Chapter 8
Different Omics Approaches in Cereals and Their Possible Implications for Developing a System Biology Approach to Study the Mechanism of Abiotic Stress Tolerance

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8.1 Introduction

Cereals comprise a number of crops including rice, wheat, maize, barley, rye and sorghum. In the form of starch and proteins, the cereal grains provide nearly 60 % of the calories consumed globally as food and fodder. There is a growing challenge to meet the global demand of food security for a human population of 9 billion expected by the year 2050 (Royal 2009; Sreenivasulu and Schnurbusch 2012). Current predicted climatic conditions such as prolonged drought and heat episodes pose a serious threat for the agricultural production world-wide, affecting yield losses estimated at billions of dollars (Mittler 2006; IPCC 2007; Battisti and Naylor 2009). Hence, increasing crop productivity in view of escalating population as well diminishing cultivable land and natural resources in such challenging environmental conditions has become a matter of urgency. Although much research has been conducted to evaluate the effects of global warming due to a variety of human activities (Smit et al. 1988), efforts to search specific and practical approaches to improve adaptability of plants to the climate change have only begun recently (Charng et al. 2006; Montero-Barrientos et al. 2010).

Abiotic stresses lead to a series of changes in the plant that affect molecular, biochemical, physiological and phenological processes eventually affecting the performance of plant growth and development impacting overall yield (Wang et al. 2003; Sreenivasulu et al. 2007). Plants that successfully withstand stresses are constantly monitoring their external milieu and are redefining the appropriate cellular response. It depends on the ability of the plants to be equipped with intricate gene regulatory mechanisms leading to the appropriate physiological adaptation to survive harsh challenging conditions. Therefore, understanding plant abiotic stress responses is

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now thought to be one of the most important topics in plant science. Different omics-approaches have been used to elucidate some of the key regulatory pathways in plant responses to abiotic stresses. The plant physiological and molecular responses to abiotic stresses have been investigated using various genomics strategies (Vij and Tyagi 2007; Collins et al. 2008; Hu et al. 2009), which include transcriptomics (Rostoks et al. 2005; Mohammadi et al. 2007; Zeller et al. 2009), proteomics (Qureshi et al. 2007; Caruso et al. 2009) and metabolomics (Shulaev et al. 2008). For a comprehensive understanding of global response we need to integrate these responses at a systems level and need to build integrative platforms to derive knowledge, which may facilitate development of stress tolerance in crop plants.

A systems biology/omics approach is a new upcoming field in plant biology, which allows not only a better understanding of molecular processes and cellular function (Kitano 2000), but also to identify the molecular targets for crop improvement (Cramer et al. 2011). One of the key challenges of systems biology is to integrate the different omics information to give a more complete picture of living organisms. Such an integrated approach would unravel the complex interplay or cross-talk between the different components and to understand the dynamic activities of a tissue/organ/organism in different environments (Cramer et al. 2011). The availability of these data in model species not only allowed a comprehensive understanding of responses against abiotic stresses, but eventually will make the way forward to identify key targets for engineering abiotic stress tolerance in cereals.

8.2 Status of Genome Sequences in Cereals

The genome sequence, often referred to as the genetic blueprint, provides a foundation for connecting the information from the genome to the phenome via structural and functional genomics with an extended approach of systems biology. The development of genomic resources has progressed in a number of plant species, thus creating the gold standard reference genomes in several crops of the grass family including rice, maize, Brachypodium and sorghum. Despite variation in genetic diversity, genome size and chromo-some number, there is substantial conservation in gene order between the grasses which is explored through the study of synteny and collinearity. Extensive data on all aspects of cereal genomics are now available at GrainGenes (http://wheat.pw.usda.gov/) and Gramene (http://gramene.org/), the latter having a major emphasis on rice genome and its syntenic relationship with other cereal genomes. Here, we briefly review the current status of available genomic sequences for cereal crop species (Table 8.1).

8.2.1 Rice

Among cereals, the first draft sequence is released in rice in two sub-species japonica and indica (the two subspecies of Asia) by the commercial effort from Syngenta, USA (Goff et al. 2002) and public academic effort by Beijing

Table 8.1 Whole genome sequencing projects in cereals

Common Name	Species	Genome size(Mbp)	Database	Sequencing group
Rice	*Oryza sativa* (japonica)	420	http://rgp.dna.affrc.go.jp/IRGSP/index.html	IRGSP
Rice	*Oryza sativa* (indica)	466	http://rice.genomics.org.cn/rice/index2.jsp	Beijing Genomics Institute
Barley	*Hordeum vulgare*	5,500	http://www.public.iastate.edu/~imagefpc/IBSC%20Webpage/IBSC%20Template-home.html	Consortium (IBSC)
Barley	*Hordeum vulgare*		http://webblast.ipk-gatersleben.de/barley/index.php	
Purple false brome	*Brachypodium*	272	http://www.brachypodium.org/	JGI, Consortium (IBI)
Maize	*Zea mays*	2,500	http://www.maizegdb.org/	Consortium
Wheat	*Triticum aestivum*	16,500	http://www.wheatgenome.org/ http://urgi.versailles.inra.fr/index.php/urgi/Projects/3BSeq http://www.cshl.edu/genome/wheat http://www.cerealsdb.uk.net/	Consortium (IWGSC)

Genomics Institute, China (Yu et al. 2002), respectively. This effort resulted in generating whole-genome shotgun (WGS) genome draft of japonica and indica, covering more than 90 % of the 420 megabase (Mb) genome and also suggested that genome size is increased by >6 % and >2 %, respectively compared to the common ancestor. Also these two sub-species showed a genetic divergence through a detection of numerous SNPs, indels within both the unique (coding) and the repetitive regions. In 2005, IRGSP released high quality map-based draft sequence in the public domain by providing indexing of 37,544 protein coding genes (International Rice Genome Sequencing Project 2002). Gene predictions developed by the Plant Genomics Group at TIGR (http://rice.plantbiology.msu.edu/) and RAP-DB released the rice genome annotation for the public use (Tanaka et al. 2008). The Rice FOX (full-length cDNA overexpressor) gene hunting system is a resource of gain-of-function mutants where 13,000 full-length rice cDNA clones are overexpressed in Arabidopsis (rice FOX Arabidopsis lines, http://ricefox.psc.riken.jp/) to characterize gene functions in a heterologous system (Kondou et al. 2009; Sakurai et al. 2011). By this way, several full-length cDNAs from rice were shown to represent function of orthologous genes in Arabidopsis as a FOX line mutant collection with interesting phenotypes (Sakurai et al. 2011).

8.2.2 Maize

Maize is an important model C_4 cereal crop that is predominantly a cross-pollinating, a feature that has contributed to its broad morphological variability and geographical adaptability. Maize genome size is estimated to be 2,500 Mb, which is six times bigger than the rice genome, owing to the expansion of families of transposable elements, particularly retrotransposons (Berhan et al. 1993). The maize genome size has expanded dramatically (up to 2.3 Gb) over the last ~3 million years via a proliferation of long terminal repeats of retrotransposons (SanMiguel et al. 1998). Comparative analysis of grass genomes also reveals conservation of gene order but some local rearrangements interrupt collinearity at molecular level (Feuillet and Keller 2002). These rearrangements often prevent maize gene cloning using other cereals genome sequence information as a reference. Thus, having completed maize genome sequencing is extremely beneficial to better understand gene and genome structure of rice and maize, and to understand the evolution of complex grass genomes. The draft genome of maize B73 has been sequenced (Schnable et al. 2009) using a minimum tiling path of bacterial artificial chromosomes (BACs) (16,848) and fosmid (63) clones derived from an integrated physical and genetic map (Wei et al. 2009), augmented by comparisons with an optical map (Zhou et al. 2009). Shotgun sequenced clones covered up to 4–6 fold genome and followed by automated and manual sequence improvement of the unique regions only, which resulted in the B73 reference genome version 1(B73 RefGen_v1). This B73 RefGen_v1 contains 855 families of DNA transposable elements that make

up 8.6 % of the genome. From the genome sequence information 32,540 protein-encoding genes and 150 microRNA (miRNA) genes were predicted from assembled B73 RefGen_v1. Exon sizes of maize genes were similar to that of their orthologous genes in rice and sorghum, but maize genes contained larger introns because of insertion of repetitive elements (Wei et al. 2009; Haberer et al. 2005). In future, exploring intraspecific gene variability and a study of the role of epigenetics and retrotransposons will remain an important exercise to resolve the hybrid vigour and plant performance in maize.

8.2.3 Brachypodium

The whole genome sequence of Brachypodium reveals that relative to other grass genomes, Brachypodium genome is compact (272 Mb), with retrotransposons concentrated at the centromeres and at the collinearity breakpoints. A total of 25,532 protein-coding genes were predicted in the v1.0 annotation. This is in the same range as sorghum (27,640) (Paterson et al. 2009). Between 77 and 84 % gene families are shared among the three grass subfamilies represented by Brachypodium, rice and sorghum, reflecting a relatively recent common origin (The International Brachypodium Initiative 2010). The similarities in gene content and gene family structure between Brachypodium, rice and sorghum support the value of Brachypodium as a functional genomics model for all grasses. The relatively small genome of Brachypodium contains many active retroelement families, but recombination between these retroelements keeps genome expansion in check. Because of small size and rapid life cycle, and its genetic proximity to tribe Triticeae, Brachypodium has several advantages. The small size of some accessions makes it convenient for cultivation in a small space. This has led to the development of highly efficient transformation systems for a range of Brachypodium genotypes (Vain et al. 2008; Vogel and Hill 2008; Alves et al. 2009). Also several important resources have been developed, which includes germplasm collections (Vogel and Hill 2008; Filiz et al. 2009; Vogel et al. 2009), genetic markers (Vogel et al. 2009), a genetic linkage map (Garvin et al. 2010), bacterial artificial chromosome (BAC) libraries (Huo et al. 2006, 2008), physical maps (Gu et al. 2009), large-scale collection of T-DNA tagged lines termed 'the BrachyTAG program' mutant collections (Thole et al. 2010), microarrays and databases (Table 8.2). These resources are facilitating the use of Brachypodium by the research community, and will allow Brachypodium to be used as a powerful functional genomics resource for grasses. Since Brachypodium is more closely related to the Triticeae (wheat, barley) than to the other cereals, Brachypodium genome also helps in the genome analysis and gene identification in the large and complex genomes of Triticeae tribe (wheat and barley), which are among the world's most important crops. It is also an important advance in grass structural genomics permitting for the first time, whole-genome comparisons between members of the three most important grass subfamilies.

Table 8.2 Omics related resources in cereals and the corresponding URLs links

S.No	Omic resources	URLs	Species
1	Transcriptomics	https://www.genevestigator.com/gv/	Plant species
		http://bar.utoronto.ca/welcome.htm	Cereals
		http://www.plexdb.org/index.php	Cereals
		http://mpss.udel.edu	Cereals
		http://contigcomp.acpfg.com.au	Wheat, barley
		http://bioinformatics.med.yale.edu/riceatlas/	Rice
2	Metabolomics	http://mapman.gabipd.org/web/guest	Cereals
		http://pathway.gramene.org/	Brachypodium, rice, maize
		http://www.genome.jp/kegg/pathway.html	Brachypodium, rice, maize
		https://www.metabolome-express.org/	Rice, wheat
		http://www.cbib.u-bordeaux2.fr/MERYB/	Rice, maize
		http://www.plantcyc.org/	Rice, maize
3	Proteomics	http://ppdb.tc.cornell.edu/	Maize, rice
		http://www.p3db.org/	Rice, maize
		https://database.riken.jp/sw/en/Plant_Phosphoproteome_Database/ria102i/	Rice
		http://cdna01.dna.affrc.go.jp/RPD/main_en.html	Rice
4	Phenomics	http://wheat.pw.usda.gov/GG2/germplasm.shtml#collections	Wheat, barley
		http://tilling.ucdavis.edu/index.php/Main_Page	Rice, wheat
		http://www.postech.ac.kr/life/pfg/risd/	Rice
		http://tos.nias.affrc.go.jp/	Rice
		http://ricefox.psc.riken.jp/	Rice
		http://orygenesdb.cirad.fr/	Rice
		http://www.shigen.nig.ac.jp/rice/oryzabase/top/top.jsp	Rice
		http://barley.ipk-gatersleben.de/ebdb/	Barley

(continued)

Table 8.2 (continued)

S.No	Omic resources	URLs	Species
		http://ace.untamo.net/	Barley
		http://barleygenomics.wsu.edu/mut-4-3-2.html	Barley
		http://www.maizegdb.org/stock.php	Maize
		http://www.brachytag.org	Brachypodium
5	Integrative omics	http://prime.psc.riken.jp/	
		http://www.phytozome.net/	Plant species
		http://www.plantgdb.org/	Plant species
		http://plants.ensembl.org/index.html	Plant species
		http://chloroplast.cbio.psu.edu/	Plant species
		http://www.genome.jp/kegg/plant/	Plant species
		http://pathway.gramene.org/expression.html	Gramineae
		http://wheat.pw.usda.gov/GG2/index.shtml	Triticeae, avena
		http://kpv.kazusa.or.jp/kappa-view/	Rice
		http://rice.plantbiology.msu.edu/	Rice
		http://rapdb.dna.affrc.go.jp/	Rice
		http://www.maizegdb.org/	Maize
7	Full-length cDNA	http://www.shigen.nig.ac.jp/barley/	Barley
		http://cdna01.dna.affrc.go.jp/cDNA/	Rice (japonica)
		http://www.ncgr.ac.cn/ricd	Rice (indica)
		http://trifldb.psc.riken.jp/	Wheat
		http://www.maizecdna.org/	Maize

8.2.4 Barley

Barley (*Hordeum vulgare* L.) ranks fourth among the cereals in worldwide production and due to its broad stress tolerance adaptability, high genetic variability and close relationship to wheat and rye, barley is considered as an excellent model C_3 crop of Triticeae (Koornneef et al. 1997; Hayes et al. 2003; Sreenivasulu et al. 2008a). Barley genome comprises seven chromosomes with estimated genome size of 5,100 Mb (12 times that of rice) of which 80 % of genome is composed of repetitive DNA, which is presently a major challenge to decipher the complete genome. The systematic efforts for sequencing the whole barley genome were initiated in 2006 by International Barley Sequencing Consortium (IBSC) (http://www.public.iastate.edu/~imagefpc/IBSC%20Webpage/IBSC%20Template-home.html) and the cultivar Morex was recommended as a reference genome. Several approaches are being used to unlock the gene content in the whole genome by next-generation sequencing of sorted chromosomes, sequencing of gene-rich BAC clones and full-length cDNA collections (Sreenivasulu et al. 2008b; Mayer et al. 2011; Schulte et al. 2011). As a result, Barley Sequencing Consortium is continuously generating voluminous sequencing data that is accessible from the website (http://webblast.ipk-gatersleben.de/barley/index.php). A novel analytical platform is also available for genome-wide SNP genotyping (9 K Infinium array) for barley and has been used to survey genomic variations among barley germplasm and to evaluate chromosomal distribution of introgressed segments of near-isogenic lines. Also several transcriptome platforms are available to generate genome wide transcriptome atlas (Druka et al. 2006, 2011; Sreenivasulu et al. 2006, 2008a). Natural variants among barley collections were used to investigate the associations between nucleotide haplotypes and growth habits that are witnessed in different geographical distribution (Saisho and Takeda 2011; Pasam et al. 2012).

8.2.5 Wheat

Wheat is the most widely grown and important staple cereal crop, which occupies more arable land (17 % of all crop area) and possesses more market share ($31 billion) than any other cereal crop (Gupta et al. 2008; Safar et al. 2010). Wheat is a hexaploid, with A, B and D subgenomes, the entire genome being 40-fold larger than the rice genome (Arumuganathan and Earle 1991) and each individual subgenome being ~5,500 Mb in size. The large genome size, hexaploid nature and a high proportion of repetitive DNA creates significant challenges in elucidating its genome sequence and to connect genome sequences to the phenotypic variance of agronomic traits (Chantret et al. 2005; Paux et al. 2008; Wanjugi et al. 2009). International wheat genome sequencing consortium (IWGSC) has began to target a complete high quality genome

sequence, by adopting a chromosome-based strategy to construct physical BAC clone maps and subsequently to sequence each of the individual chromosomes (Dolezel et al. 2007). In this context, around 68,000 BAC clones of a 3B chromosome-specific BAC library (Safar et al. 2004; Paux et al. 2008) have been fingerprinted at the French National Sequencing Centre and the sequencing of these BAC clones is under progress (http://urgi.versailles.inra.fr/index.php/urgi/Projects/3BSeq). Several approaches have been initiated to sequence the complex wheat genome. For instance, the consortium from UK produced 5X sequence of the bread wheat genome using Roche 454 technology (http://www.cerealsdb.uk.net/), and also produced a draft wheat genome assembly from the donor species of the wheat D genome, *A. tauschii* (http://www.cshl.edu/genome/wheat). Sequences from individual flow-sorted bread wheat chromosome arms are also piling up gradually (Berkman et al. 2011; Wicker et al. 2011). With the increased availability of wheat genome sequence data, it is necessary to provide resources that can integrate wheat-specific sequence information to become useful for crop improvement (Edwards and Batley 2010). Since wheat genome sequencing is still in progress, and a high quality genome sequence is expecting by 2015, one can foresee the possibilities of launching systems biology approaches even in barley and wheat. These systematic attempts to move from genomic to post-genomic strategies greatly facilitate researchers who wish to use this information to improve this valuable crop. The update about the genome sequencing project information and other genetic resources are listed in the Table 1.

Evaluating the impact of genome organization, monitoring dynamic alteration of retrotransposons, assessing the impact of epigenetic hallmarks by covering genome wide DNA methylation and omics driven systems biology approaches are all part of genome dynamic applications. In this review we focus on transcriptome, proteome and metabolome data available in cereals and other model species. Further we discuss the future needs of implementing systems biology applications to derive work flow to identify key target genes for crop improvement.

8.3 Omics Revolution by High Throughput Approaches

Major progress made in the last decade is through the use of new high-throughput techniques not only in the field of whole genome sequencing but also through characterization of genes through functional genomics. Systematic use of different omics approaches such as transcriptomics, proteomics, metabolomics, fluxome and a way forward to connect the global data to the phenotypic variance (generated through phenomics) have led to expand the area towards systems biology for elucidating the mechanisms underlying the expression of agronomic traits. System-based approaches based on a combination of multiple omics analyses has been an efficient approach to determine the global picture of cellular systems and to reveal the plant responses and adaptation to a specific stress. In this context, the integrated approaches with multiple-omics data should contribute greatly to the

identification of key regulatory steps and to characterize the pathway interaction in various processes. These illustrative examples demonstrate the power of multi-omics-based systems analysis for understanding the key components of cellular systems underlying various plant functions. The integration of a wide spectrum of omics datasets from various plant species is then essential to promote translational research to engineer plant systems in response to the challenges of emerging climate change.

8.3.1 Transcriptomics

Genome-wide transcriptome profiling is a powerful approach to assemble a transcriptome atlas of expressed genes involved in various biological phenomena and to reveal the molecular cross-talk of gene regulatory networks of responses to various abiotic stresses. Microarray analysis is known to be an important approach to elucidate the molecular basis of the plant stress response (Van Baarlen et al. 2008; Deyholos 2010). The investigation of gene expression related to several physiological and agronomical traits have been reported in different cereals. These responses include the following: responses to hormones (Seki et al. 2002b; Rabbani et al. 2003), various stress responses (Kreps et al. 2002; Rabbani et al. 2003; Takahashi et al. 2004), including drought (Kreps et al. 2002; Oono et al. 2003; Rabbani et al. 2003), cold (Kreps et al. 2002; Rabbani et al. 2003; Yamaguchi et al. 2004), high light (Rossel et al. 2002; Kimura et al. 2003), hyperosmolarity, oxidative stress (Takahashi et al. 2004), and iron deficiency (Thimm et al. 2001).

More detailed and comprehensive gene expression studies have been conducted in the model species like *Arabidopsis* and rice, and the resulting knowledge can be used in cereals through comparative gene networks. In case of cereals, several data repositories have been created to store the raw data and normalized expression values generated from GeneChip arrays including Affymetrix 57 K from Rice, 61 K Wheat, 22 K Barley1, full-genome Brachypodium and Maize arrays. Furthermore, these databases not only allow storage of data from Affymetrix platform but also allow storing data from Agilent and NimbleGen platforms (Sreenivasulu et al. 2010). These databases include PLEXdb, GEO, Genevestigator, UniProt, PlantGDB (Bombarely et al. 2011) Gramene (Youens-Clark et al. 2011), TAIR (Swarbreck et al. 2008) and MaizeGDB (Schaeffer et al. 2011).

Transcriptome studies have also been carried out in cereals and other model plants but mainly applying single stress at a time such as drought, salinity, cold or heat during the vegetative state (for recent reviews see Ingram and Bartels 1996; Sreenivasulu et al. 2004a, 2007; Kishor et al. 2005; Vij and Tyagi 2007; Fleury et al. 2010). Interestingly, unique stress responsive pathways such as osmolyte metabolism, antioxidant machinery, dehydrin and LEA proteins, chaperones and gene machinery involved in protection of cell integrity are preferentially upregulated in both dicots and monocots (Xue et al. 2006; Ergen et al. 2009; Fleury et al. 2010; Sreenivasulu et al. 2010). However, within osmolyte metabolism, wide

array of biochemical pathways are known to activate preferentially in a species and genotype specific manner, which corresponds to compounds proline, mannitol, myo-innositol, trehalose, glycine metabolism, accumulation of sugar alcohols and free sugars including fructose metabolism. Additionally, some studies have identified abundance of various transcripts during heat treatment, including genes encoding for galactinol synthase and enzymes in the raffinose oligosaccharide pathway, and antioxidant enzymes (Lim et al. 2006; Xu et al. 2007). Comparison of transcript profiles between tolerant and susceptible lines under various stress responses has revealed differences in stress-responsive pathways reflecting difference in physiological response and adaptation behavior. Transcriptome analysis also revealed some unexpected results such as a decrease in the expression of glutathione-related genes following withholding of water in a tolerant synthetic wheat line (Mohammadi et al. 2007), or the accumulation of proline in a drought-sensitive emmer wheat line (Ergen and Budak 2009), suggesting that some pathways/mechanisms are dependent upon genotype, the duration, intensity, and type of stress applied. There are some reports, which show decrease in transcript abundance related to programmed cell death, basic metabolism, and biotic stress responses (Larkindale and Vierling 2008) under heat stress conditions. Recently, Pinheiro and Chaves (2011) reviewed 450 research papers on drought-mediated changes in photosynthesis.

Until now most of the transcriptome responses have been studied in vegetative tissues and recently few attempts were made to reveal the transcriptome alterations in developing seeds to understand the yield stability. In case of cereals, transcriptome analyses were recently applied to analyze rice developing caryopses under high temperature conditions (Yamakawa and Hakata 2010) and seed developmental alterations in barley under drought (Worch et al. 2011). Overall, several extensive attempts have been made to identify several genes/pathways in a number of cereal crops including rice (Amudha and Balasubramani 2011; Hadiarto and Tran 2011; Yang et al. 2010). However, any deeper and/or new insights into mechanisms of the function of genes were missing. In combination with these reviews, the present review of literature based on transcriptome studies should present a pertinent update on genes involved in abiotic stress tolerance in crop plants. The effort is to lend a perspective on how different pieces may fit into the complicated puzzle and to present the integrated view on abiotic stress tolerance.

8.3.2 Proteomics

Although transcriptomics data provides an useful overview of global gene expression regulation, proteomics is often used as a complementary technique that provides the actual state of the condition of cell response to stress. Moreover, proteomics is considered as an essential bridge between the transcriptome and the metabolome (Wasinger et al. 1995; Zhu et al. 2003). Compared to transcriptome

analysis, proteomics approach has a close relationship to phenotype because of their direct action on several biochemical processes. This approach is important in evaluating stress responses since the mRNA levels may not always correlate with protein accumulation (Gygi et al. 1999) and moreover several regulatory proteins are subjected to proteolysis to fine tune the dynamics of transcribed machinery. Despite this strategic importance, compared to transcriptomics analysis, plant proteome response to abiotic and biotic stresses is still limited.

In the last decade, good progress has been made in the separation of proteins and their identification by mass spectrometry. Studies have evaluated changes in protein levels of plant tissues in response to stresses (Canovas et al. 2004; Kim et al. 2003). However, these studies have mainly focused on model species such as Arabidopsis and rice (Canovas et al. 2004). Implication of proteomic studies in cereals is mainly based on rice as a model species (Agrawal and Rakwal 2006, 2011; Komatsu and Yano 2006). A proteomic analysis of drought and salt-stressed rice plants found that around 3000 proteins could be detected in a single gel and over 1,000 could be analyzed (Salekdeh et al. 2002). The effect of salt stress on young rice panicles has been investigated by the same group (Dooki et al. 2006). The proteomic analysis of rice leaf sheaths during drought stress identified 10 up-regulated and two down-regulated proteins. Among the up-regulated proteins, one was an actin depolymerizing factor present at high levels in the leaves of non-stressed drought-resistant cultivars (Ali and Komatsu 2006). Proteome reference maps have been compiled for maize (Mechin et al. 2004) and wheat (Vensel et al. 2005) endosperm and for barley grain (Finnie et al. 2002) during the processes of grain filling and maturation. The effect of heat stress on the grain of hexaploid wheat has been thoroughly studied at the protein level and down-regulation of several proteins involved in the starch metabolism and the induction of HSPs was reported (Majoul et al. 2003, 2004). The effect of drought on the wheat grain proteome, involved 121 proteins that exhibited significant changes in response to the stress; 57 of these 121 proteins could be identified (Hajheidari et al. 2007). Two-thirds of the identified proteins turned out to be thioredoxin targets, revealing the link between drought and oxidative stresses. Changes in the protein complement have been monitored in maize under progressive water deficit and several genes/proteins were reported to be involved in the drought response (Riccardi et al. 1998). The high level of genetic variability observed at the proteome level for the drought response in maize (de Vienne et al. 1999) allowed identification of *Asr*1 (ABA/water-stress/ripening-related1) gene as a candidate for genetic improvement (Jeanneau et al. 2002). Apart from this, some proteomics resources are also available for grasses, such as the plant proteome database (http://ppdb.tc.cornell.edu/) which provides information on the maize and *Arabidopsis* proteomes. RIKEN Plant Phosphoproteome Database (RIPP-DB, http://phosphoproteome.psc.database.riken.jp) was updated with a data set of large-scale identification of rice phosphorylated proteins (Nakagami et al. 2010, 2012). The OryzaPG-DB was launched as a rice proteome database based on shotgun proteomics (Helmy et al. 2011). Although only a handful of studies have been carried out in cereal

crops, it is expected to have a significant increase in the implementation of these techniques in cereal crops to study genome wide protein–protein interactions.

8.3.3 Metabolomics and Fluxome

Metabolomics is one of the important component of functional genomics. It defines the quantitative metabolite signatures present in a cell/tissue under a given set of physiological conditions (Oliver et al. 1998; Kell et al. 2005; Jordan et al. 2009). Higher plants have the remarkable ability to synthesize a vast array of compounds that differ in the chemical complexity, structure and biological activity, playing indispensable roles in chemical defenses against biotic and abiotic stresses (Verpoorte and Memelink 2002; Dixon and Strack 2003; Schwab 2003). Moreover, under various stress conditions, crop species are known to modulate the primary metabolism due to the impaired photosynthesis and respiration events. The main advantage of metabolomics is that it allows one to measure the impact of metabolism and to interlink the key metabolic signatures to the phenotype.

Study of metabolic regulation during stressful conditions has been facilitated through mass spectrometry-based analytical methods resulting in the detection and identification of diverse metabolites (Sawada et al. 2009). Metabolite profiling deals with detection of a wide range of metabolites in diverse concentrations, which makes their analysis more complicated. Therefore, more comprehensive coverage can only be achieved by using multi-parallel complementary extraction and detection technologies subjected to chemical analysis using liquid and gaseous chromatography-mass spectrometry (LC–MS and GC–MS), nuclear magnetic resonance (NMR) and Fourier transform-infrared spectrometer (FT-IR).

Metabolome analyses of model plants have markedly increased in the recent decade and helped to understand the plant response to various stresses. To obtain deeper view into cellular conditions under abiotic stresses, metabolomic investigations have been performed initially in model species like *Arabidopsis* and other plant species (Schauer and Fernie 2006). From the genome sequence information of the *A. thaliana*, it is evident that plants appear to re-organize their metabolic network in order to adapt to such conditions (Kaplan et al. 2004). Therefore, metabolomics plays a key role in understanding cellular functions and decoding the functions of genes under challenging abiotic stress conditions (Fiehn 2002; Bino et al. 2004; Oksman-Caldentey and Saito 2005; Hall 2006; Schauer and Fernie 2006; Hagel and Facchini 2008; Saito et al. 2008). Metabolic adjustments in response to different stress conditions are dynamic and multifaceted because of their intensity and nature of the stress, but it also depends on the cultivar and the type of plant species. This approach also covers the extensive comprehensive metabolite analyses, illustrating the complexity of metabolic adjustments to different abiotic stresses (Rizhsky et al. 2004; Urano et al. 2009) including salinity (Cramer et al. 2007; Kempa et al. 2007; Sanchez et al. 2008; Janz et al. 2010; Lugan et al. 2010), and temperature stress (Cook et al. 2004; Rizhsky et al. 2004;

Kaplan et al. 2007; Usadel et al. 2008; Espinoza et al. 2010; Caldana et al. 2011). Some metabolic changes are common to salt, drought, and temperature stress, whereas others are specific to particular stress (Gong et al. 2005; Cramer et al. 2007; Gagneul et al. 2007; Kempa et al. 2008; Sanchez et al. 2008; Usadel et al. 2008; Urano et al. 2009; Lugan et al. 2010). Metabolomic profiles illustrate that plants have developed a wide range of strategies to adapt their metabolism to unfavorable growth conditions and that enhanced stress resistance is not restricted to a single compound or mechanism. Several metabolites/metabolic pathways that contribute to stress acclimation also play a role in development (Hanzawa et al. 2000; Samach et al. 2000; Eastmond et al. 2002; Palanivelu et al. 2003; Imai et al. 2004; van Dijken et al. 2004; Alcazar et al. 2005; Gupta and Kaur 2005; Satoh-Nagasawa et al. 2006; Mattioli et al. 2008, 2009; Szekely et al. 2008; Deeb et al. 2010; Zhang et al. 2011).

Surprisingly, metabolomic research has made a limited progress in cereals. A recent metablolome study in rice identified 88 metabolites from the extract of leaves. It was found that sugar and amino acid metabolism is dynamically altered under stress treatment (Sato et al. 2008). Metablolome study from maize kernels showed wide range of natural variability based on the influence of genetic background and growing season (Reynolds et al. 2005), developmental stages (Seebauer et al. 2004) and environment (Harrigan et al. 2007). Metabolome study of diverse maize genotypes recently explored and highlighted the importance of grain fatty acid methyl esters, free fatty acid methyl esters, free amino acids. Around 167 metabolites were identified from 300 distinct analytes by using GC–MS approach (Rohlig et al. 2009). Integrated metabolome and transcriptome analysis has also been applied to investigate changing metabolic systems in plants growing in field conditions, such as the rice Os-GIGANTEA (Os-GI) mutant and transgenic barley (Kogel et al. 2010; Izawa et al. 2011). The application of metabolomics in cereals has just begun, and its full potential will be realized only in future. Large-scale metabolic analyses are therefore necessary to observe the metabolic networks important for plant growth and development under a range of environmental conditions.

Measurement of metabolism-wide fluxes through steady-state metabolic flux balance analysis (MFA or FBA) by measuring ^{13}C redistribution signatures within the primary metabolism at subcellular compartment level, and the information about the biomass composition and growth rate generate data, which is collectively described as Fluxome. Predicted flux maps is an important part of metabolic engineering (Becker et al. 2007). Recently, several methods are refined to predict metabolic networks that determine the fluxes, which directly report on cellular physiology. The most widely used approaches for fluxome analysis are based on GC–MS measurement of labelling pattern of metabolites from the tracer studies. This approach is optimized and applied to move from gaining information of static metabolic signatures to end products. A recent approach to the fluxome consists of the comprehensive determination of enzyme activities from cyclic robotic assays and determination of the activity of each reaction step in the metabolic pathway (Gibon et al. 2006; Osuna et al. 2007). The most direct information

of metabolic regulations can be obtained through the determination of an actual metabolic flux. This method also allows gaining precise knowledge of metabolic physiology and its engineering (Christensen and Nielsen 2000; Des Rosiers et al. 2004). A range of different MFA methods has been applied to plant systems, resulting in identifying unique insights into the operation of plant metabolic networks. Implementing the emerging MFA methods for plant studies faces considerable hurdles because of the greater complexity of plant metabolic networks and our ignorance of understanding the biochemical pathway and kinetics at sub-cellular compartment levels (Sweetlove et al. 2008). For metabolic flux calculation, the different labelling data obtained are usually utilized to globally fit the unknown flux parameters by a computer flux model combining isotopomer and metabolite balancing strategies (Wiechert et al. 2001; Kiefer et al. 2004; Wittmann et al. 2004; Frick and Wittmann 2005). It has been recognized that better optimization of experimental designs is essential for distinguishing activities between parallel metabolic pathways operative in distinct cellular compartments, such as cytosol and plastids (Allen et al. 2007; Kruger et al. 2007; Li et al. 2008). Overall, MFA and dynamic labeling methods are instrumental for quantifying metabolic fluxes of plant responses under ambient and challenging environments (Roscher et al. 2000; Boatright et al. 2004; Matsuda et al. 2005; Ratcliffe and Shachar-Hill 2006; Matsuda et al. 2009). Recently, genome wide metabolic fluxes have been predicted in *Arabidopsis* for high temperature and hyperosmotic stress, so that it was possible to identify key signatures such as severe reduction in carbon-use efficiency through reduction in PEP flux and increased TCA cycle for altered growth rate (Williams et al. 2010). Fewer studies have applied MFA in cereals. In maize, fast-growing excised root tips were used to study the central carbon metabolism by keeping them for 12–18 h in a medium containing ^{13}C-labeled glucose (Dieuaide-Noubhani et al. 1995; Edwards et al. 1998), and then analyzing the most abundant labeled free intracellular metabolites (i.e., sugars and amino acids) by NMR or MS; large flux maps of central carbon metabolism were derived in this manner (Dieuaide-Noubhani et al. 1995; Alonso et al. 2005). In other studies ^{13}C labeled glucose was used to label maize kernels and barley caryopsis, and label was analyzed in both glucose (derived from starch) and amino acids (derived from proteins) available in the starchy endosperm (Glawischnig et al. 2001, 2002; Grafahrend-Belau et al. 2009; Rolletschek et al. 2011).

8.3.4 Role of Hormones

Abiotic stress response involves a trigger of similar set of transcription factors involved in both ABA-dependent and ABA-independent manner in both dicotyledonous and monocotyledonous plants (reviewed by Sreenivasulu et al. 2007). Genes differentially regulated in *Arabidopsis* and rice in response to drought, salinity and cold stress comprise gene-sets enriched with DRE-related and ABRE core motifs. Therefore both ABA-dependent and ABA-independent

signaling pathways are important in regulating the transcriptome responses (Seki et al. 2002a, 2001; Gomez-Porras et al. 2007). Abscisic acid (ABA) remains the best-studied hormone for plant stress response. However, other hormones such as cytokinins, auxins, gibberellins, brassinosteroids, strigolactones, jasmonic acid, salicylic acid as well as the gaseous hormones, ethylene and nitric oxide are being studied for their role in abiotic stress response in the recent past. Hence, we need to understand the manipulation of the phytohormone synthesis and action across the plant life-cycle, which is an attractive avenue to understand and engineer abiotic stress tolerance. In barley, the response to salinity stress includes the synthesis and the induction of the jasmonate signalling transduction pathways (Walia et al. 2006, 2007). Recently, modification of cytokinin expression, with the critical difference in the use of a stress and maturation-induced promoter in rice resulted in elevating drought tolerance to produce higher yield under stress (Peleg et al. 2011). The observed differences in the content of other phytohormones in the cytokinin-modulated transgenic rice lines also suggested synergistic or antagonistic interactions between auxins, ethylene, cytokinins and ABA in regulating stomatal behavior. Furthermore, gibberellins and brassinosteroids have a strategic importance in tolerance to a variety of abiotic stresses (Peleg and Blumwald 2011). Critical alteration in the ratio of cytokinins and abscisic acid and its antagonistic responses is known to alter the growth dynamics under abiotic stress response (Nishiyama et al. (2011). Also, the effects of three different phytohormones auxin, ABA and cytokinins on the single trait of nitrogen acquisition were reported in a recent review (Kiba et al. 2011). Nitrogen acquisition and remobilization is an important trait to be considered in abiotic stress tolerance to fine tune source-sink relationships in enhancing grain yield (Seiler et al. 2011; Kohli et al. 2012).

8.3.5 Phenomics

Phenomics involves comprehensive capture of a plant's phenotype that helps to explore the germplasm. Unfortunately, there is a large gap in our understanding of events that may occur when genotype is translated into phenotype; there is an urgent need to fill this gap (Zamboni and Sauer 2004; Furbank and Tester 2011). Plant genomes possess great plasticity in the genomes for producing various types of phenotypes. However, the genetic variability that may prove useful for developing stress tolerant lines is limited.

There are large number of initiatives launched (IPPN: International Plant Phenomics Network; DPPN: Deutsches Pflanzen Phänotypisierungs Netzwerk; EPPN: European Plant Phenotyping Network; APPF: Australian Plant Phenomics Facility) to create phenotyping facilities to screen populations, GMO material and mutant collections by employing high end image capture technologies in the phytotrons and glass houses. The Plant Accelerator (Lemnatech scan analyzer 3D) which takes non-destructive measurements of plant biomass (Finkel 2009) can also be

used. The core of the Plant Accelerator's phenotyping facility also measures level of watering and nutrient supplementation control, managing plant movement and tracking, and records images of plants in a range of different wavelengths, thus providing enormous information about the diversity of phenotype. Visible cameras quantify overall plant morphology, size, colour, shoot mass and other physical characteristics; near infra-red cameras detect water content of the leaves and soil; far infra-red provides information about leaf temperature and transpiration rate. While UV detects chlorophyll fluorescence, the GFP fluorescence will be helpful to monitor transgene expression. The first phenomics study was the use of quantitative phenotypic assays to measure salt tolerance traits such as osmotolerance Na^+ exclusion and Na^+ tissue tolerance in the diploid wheat *T. monococcum* (Rajendran et al. 2009). The advantage of this approach is that it is non-invasive, allowing other omics approaches to analyze cell products from the same plant. Also other non-invasive techniques such as magnetic resonance imaging, high resolution based nuclear magnetic resonance and positron emission tomography are implemented to gain insights into structure–function relationship (reviewed by Mir et al. 2012). To fully explore the genotype dependent tolerance mechanisms within the breeding programs, field-based high-throughput phenotyping platforms are essential to monitor the canopy temperature using infrared thermography. Furthermore, implementations of remote sensing technologies are essential to fully explore phenotypic plasticity at the field level. To explore the key agronomic traits for the improvement of sustainable agriculture, one needs to expand the systematic phenotyping to explore allelic variation in mapping populations, breeding programs and large scale mutants and GMO collections.

8.4 Integrative Systems Biology

Integration of the different omic approaches in the area of abiotic stress tolerance allows more robust identifications of molecular targets for future biotechnological applications in crop plants. Manipulating plant metabolism to better serve the future needs requires an improved understanding of the links between genotype and phenotype. Therefore, the massive omics data created from multifaceted platforms of genome, transcriptome, proteome, metabolome, flux and enzyme kinetics (Table 8.2 and Fig. 8.1) need to be interlinked to the cellular phenotype to understand the cellular physiological status under perturbed environmental conditions (Sauer et al. 1999). To address the missing links between molecules and physiology, different approaches of systems biology are implemented which includes "top–down" and "bottom–up" strategies. The major strengths of top-down systems biology are to gain an integrative view of the huge collection of omic data sets like transcriptomics and/or proteomics, metabolomics and fluxomics (Westerhoff and Palsson 2004). Top–down systems biology identifies molecular interaction networks on the basis of correlated molecular behavior observed through genome-wide 'omics' studies. Also, bottom-up systems biology deduces the functional properties that could emerge from a subsystem that has been characterized to a

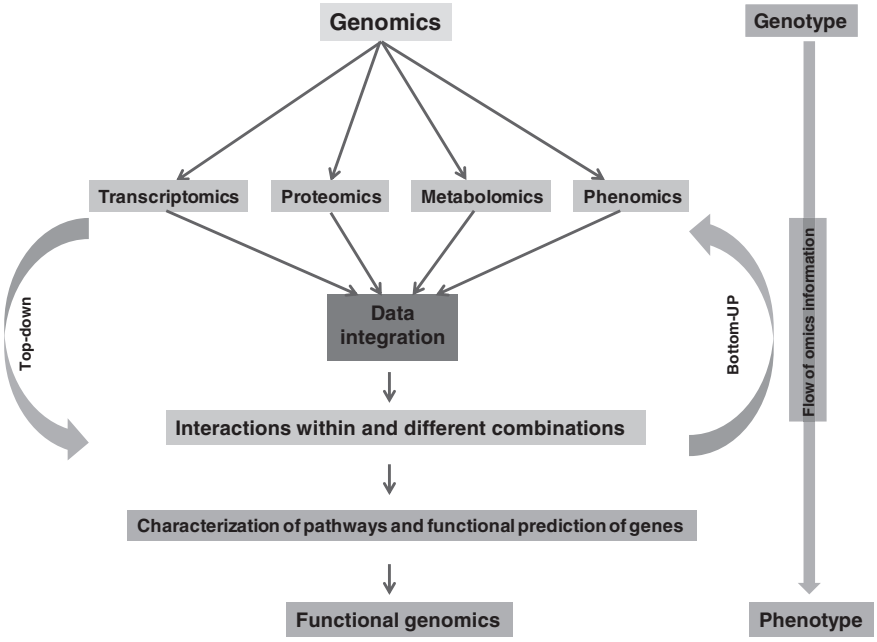

Fig. 8.1 Schematic representation of omics integration pipeline used in systems biology srategies

high level of mechanistic detail using molecular methods but focuses at the cellular level. By employing the systems biology tools in plant science, many abiotic stress-inducible genes were identified and their functions were precisely characterized in the model species.

Also, top–down systems biology concerns the identification of the structure of the molecular network that underlies system behavior that is, 'reverse engineering' from system data alone. Top–down approach starts by (re)constructing a possible topology of the network at a low level of complexity and provides a broad overview of the system at low resolution. Transcriptional networks through reverse engineering methods from the collections of gene expression data have been well pioneered on single-cell organisms, but have increasingly been applied to higher order organisms including plants where applications of systems biology methods are now emerging (Carro et al. 2010; Carrera et al. 2009; Needham et al. 2009). The available network models are mainly based on Boolean, Relevance, or Bayesian networks or association rules (Hache et al. 2009). These network inference methods are categorized into (1) those that aim to influence the genes in the general manner to influence the expression of other genes by forming gene regulatory networks (Bansal et al. 2007; Marbach et al. 2010) and (2) those, which aims to having physical interaction between transcription factors and the regulatory genes/motifs by forming the gene regulatory networks (Styczynski and Stephanopoulos 2005). The metabolic

network reconstructions that are normally done at the genome-scale are the key factors to characterize the genotype to phenotype relationships using all sequence and functional annotation data that is available in public databases combined with manual curation using the available literature and experimental data (Feist et al. 2009). Most systems biology studies have been implemented in the model plant *Arabidopsis*, where large transcriptomics programs have generated adequate quantities of high-quality data to enable systems analysis (Krishnan et al. 2009). The resulting knowledge can be used in cereals through comparative gene networks. Therefore, it is important to perform parallel studies in cereals with other characteristics, as well as to develop methods to allow use of data from the *Arabidopsis* system to conduct studies in other plant species.

Integration of different multiple 'omics' data is required to reconstruct complex networks that characterize the phenotypes in the cell (Moles et al. 2003; Kremling et al. 2004). In particular, transcriptome co-expression analysis for delimiting genes of interest has been implemented more efficiently using publicly available large transcriptome datasets such as AtGenExpress (Schmid et al. 2005; Goda et al. 2008) and NASCArrays (Craigon et al. 2004), which contain data from >1000 microarrays from model species alone. This kind of in-depth data is yet to be generated among cereal species to elucidate gene regulatory networks. The current status of available resources related to integrated databases for cereal crop species are listed in the Table 2. Transcriptome data sets are now available for co-expression analysis of the transcriptome in cereal crops; for instance, RiceArrayNet and OryzaExpress databases provide web-accessible co-expression data for rice (Lee et al. 2009; Hamada et al. 2011). The ATTED-II database also provides co-expression data sets for rice in addition to those for *Arabidopsis* (Obayashi et al. 2007; 2011). A co-expressed barley gene network was recently generated and then applied to comparative analysis to discover potential Triticeae- -specific gene expression networks (Mochida et al. 2011). PlaNet (http://aranet.mpimp-golm.mpg.de/), a database of co-expression networks for *Arabidopsis* and six plant crop species, uses a comparative network algorithm, NetworkComparer, to estimate similarities between network structures (Mutwil et al. 2011). This platform integrates gene expression patterns, associated functional annotations and MapMan term-based ontology, and facilitates knowledge transfer from *Arabidopsis* to crop species for the discovery of conserved co-expressed gene networks. The KEGG PLANT Resource (KEGG; http://www.genome.jp/kegg/) is one of the most widely established integrated database which provide information on primary metabolism of biosynthetic pathways. It aims to integrate genomic information resources with the biosynthetic pathways of natural plant products (Masoudi-Nejad et al. 2007). Another information resource for biosynthetic pathways, PlantCyc platform has been used for a number of plant species to analyze the computational analysis of the genes, enzymes, compounds, reactions and pathways involved in developmental and stress response. The pathways section in the Gramene databases provides RiceCyc, MaizeCyc, BrachyCyc and SorghumCyc, for rice, maize, Brachypodium and sorghum, respectively (http://www.gramene.org/pathway/). These resources will enable cereal workers to focus on active analysis of regulatory networks that

may be involved in different biological functions (de la Fuente et al. 2002; Vlad et al. 2004; Kholodenko et al. 2002).

Generally, a preselected set of genes designated as guide genes or bait genes for the core part of the network modules is computed for co-expression with other genes for the generation of co-expression networks (Horan et al. 2008). If a network frame is formed between unknown and known genes, it is presumed that these genes share a common regulatory system and thus are involved in the same pathway. This approach was applied for identification of genes involved in several biochemical pathways such as cellulose synthesis (Persson et al. 2005), aliphatic glucosinolate biosynthesis (Hirai et al. 2007), glucosinolate biosynthetic pathway (Hansen et al. 2007; Geu-Flores et al. 2009) and hormone metabolism (Goda et al. 2008). In case of cereals, the integrated analysis of metabolome and transcriptome was recently conducted to analyze rice caryopses developing under high temperature conditions (Yamakawa and Hakata 2010); molecular events underlying pollination-induced and pollination-independent fruit sets were also examined (Wang et al. 2009). Integrated analysis of metabolome and transcriptome has also been applied to investigate changing metabolic systems in field grown plants of rice Os-GIGANTEA (Os-GI) mutant and transgenic barley lines (Kogel et al. 2010; Izawa et al. 2011). An integrated analysis of proteome and metabolome was also used to compare the differences in response to anoxia between rice and wheat coleoptiles (Shingaki-Wells et al. 2011). Furthermore, an integrated analysis of transcriptome, proteome and metabolome was conducted to characterize the cascading changes in UV-B-mediated responses in maize (Casati et al. 2011). In this context, the integrated approaches with multiple omics data should contribute greatly to the identification of key regulatory steps and to characterize the pathways for various processes. Following these successful efforts, multi-omics-based systems analyses have improved our understanding of plant cellular systems by integrating metabolome analysis with genome and transcriptome resources (Hirai et al. 2004; Saito et al. 2008; Okazaki et al. 2009). The URLs of each integrative database in plant genomics are listed in Table 2.

The main objective of the above strategy is to discover new molecular mechanisms using an iterative cycle that starts with experimental data, followed by data analysis and data integration to determine correlations between the molecules. As an end process, the formulation of hypotheses concerning co- and inter-regulation of groups of those molecules will be revealed. The omics data obtained under a specific condition such as stress response from a given gene knockouts are used for integrated omics analysis in this strategy. Such an analysis allowed the prediction of functional relevance of key genes involved in stress-specific regulons determining tolerance. This approach has become the key to decipher the functional analysis of the genes identified from the whole genome sequencing of the plants. Alternatively, it also helps to identify ubiquitous stress regulated pathways. However, more attention is now focused in the creation of mutants and screening the response to abiotic stress using multi-layered omics strategy. To date, more than half a million T-DNA mutants have been developed for rice and *Arabidopsis* (An et al. 2005; O'Malley and Ecker 2010). In other cereals, like Brachypodium, a large-scale collection of T-DNA tagged lines termed 'the BrachyTAG program' have been developed and

used to investigate gene functions (Thole et al. 2010). A collection of several knockout mutants in cereals has been generated to assess the function of genes involved in abiotic stress. The rice full-length cDNA overexpressed *Arabidopsis* mutant database (Rice FOX Database, http://ricefox.psc.riken.jp/) was a new information resource for the FOX line (Sakurai et al. 2011). The system was also used to screen salt stress-resistant lines in the T_1 generation produced by the transformation of 43 focused stress-inducible transcription factors of *Arabidopsis* (Fujita et al. 2007). Then, the system was applied to a set of full-length rice cDNA clones aiming for *in planta* high-throughput screening of rice functional genes, with *Arabidopsis* as the host species (Kondou et al. 2009). Thus, the FOX hunting system is capable of the high-throughput characterization of gene functions. Furthermore, in rice, the endogenous retrotransposon *Tos*17, which is activated in particular conditions, is also available for the study of the insertion mutant lines of a *japonica* rice cultivar, Nipponbare (Miyao et al. 2007). Several mutants were isolated in wheat, which showed increased resistance towards biotic stress tolerance. In wheat, heat tolerant (Mullarkey and Jones 2000) and salt tolerant plants (Huo et al. 2004) have already been charecterized to study the genetic basis of stress tolerance. Additionally, the maize *Enhancer*/*Suppressor Mutator* (En/*Spm*) element has also been used as an effective tool for the study of functional genomics in plants (Kumar et al. 2005). Other approach to study the gain-of-function of mutations by activation tagging have been developed and performed in *Arabidopsis*, rice and soybean (Weigel et al. 2000; An et al. 2005; Kuromori et al. 2009). The current status of available resources related to mutants database for cereal crop species were listed in the Table 8.2.

8.5 Identification of Key Candidate Genes for Tolerance to Abiotic Stress and Validation of their Functions Using Transgenic Approaches

One of the key challenges facing agriculture today is the acute water shortage and high temperature caused by worldwide climate change and the increasing world population. Fulfilling the needs of this growing population is quite difficult from the limited arable land area available on the globe. Although there are legal, social and political barriers to the utilization of biotechnology, advances made in this field have great potential to substantially improve agricultural productivity under challenging environments. Both non-GMO and GMO strategies have been implemented to improve tolerance in crop plants. Genetic engineering is thus being intensively explored to improve plant tolerance to various abiotic stresses, and transgenic crop genotypes with improved stress resistance have actually been produced (Bartels and Sunkar 2005; Vinocur and Altman 2005; Umezawa et al. 2006; Pennisi 2008; Wan et al. 2009). In case of maize, drought tolerance transgenics are also undergoing field trails in Africa, and some other drought tolerant genotypes are also being used by the farmers for commercial cultivation. Performance of a number of other events in maize and other crops are being subjected to field trials. Partial drought

tolerance has been achieved in the vegetative phase through gene transfer by altering the accumulation of osmoprotectants, production of chaperones, protection of cell integrity by expression of LEA proteins and improved superoxide radical scavenging mechanisms (see reviews by Hasegawa et al. 2000; Kishor et al. 2005; Sangam et al. 2005; Sreenivasulu et al. 2004b, 2007; Vij and Tyagi 2007). In addition, overexpression of the key regulators ABF2, ABF3 and ABF4 of Arabidopsis involved in ABA-dependent signaling as well as constitutive expression of the Arabidopsis DREB1A, DREB1B, DREB1C and DREB2A transcription factors participating in ABA-independent signaling pathways have been shown to be effective in engineering drought tolerance (see reviews by Agarwal et al. 2006; Umezawa et al. 2006; Sreenivasulu et al. 2007). Genetic engineering strategy has been successfully applied to increase tolerance against a number of other abiotic stresses also. In this context, a variety of crops from cereals (rice, maize, barley, Brachypodium and wheat etc.,) have been engineered for enhanced resistance to a multitude of stresses, each individually, or in combination of biotic and abiotic stresses. Enhancing plant tolerance to abiotic stresses involves multiple mechanisms and therefore involves manipulation of different physiological and biochemical pathways (Wang et al. 2003; Zhang et al. 2009).

8.6 Summary and Outlook

The availability of complete genome sequence information of model species like *Arabidopsis thaliana*, *Oryza sativa* and other cereal plants has made valuable contributions in dissecting the stress response at the level of transcriptional regulation, post-transcriptional, post-translational modifications and epigenetic regulation. Using high throughput modern techniques like transcriptomics, metabolomics and proteomics, stress-responsive pathway genes have been identified. These strategies enabled us to identify key stress regulators by deriving complicated regulatory network. Employing the systems biology tools in plant science, many abiotic stress-inducible genes were identified and their functions were precisely characterized in the model species.

The identification of stress-regulators gave rise to the idea that plants have developed flexible cellular response mechanisms to efficiently respond to various abiotic stresses. Numerous genes that are induced by various abiotic stresses have been identified using various microarray systems and these gene products are classified into two groups. The first group includes proteins functioning in direct abiotic stress tolerance; these include the following: chaperones, LEA proteins, osmotin, antifreeze proteins, mRNA-binding proteins, key enzymes for osmolyte biosynthesis such as proline, water channel proteins, sugar and proline transporters, detoxification enzymes, and enzymes involved in fatty acid metabolism, proteinase inhibitors, ferritin, and lipid-transfer proteins. The second group includes factors involved in regulatory function related to signal transduction, hormonal response and transcription factors, which are responsive to various stress factors. These transcription factors could regulate various stress inducible genes cooperatively or independently, and may constitute gene networks.

Under drought, photosynthesis is affected by decreased intake and diffusion of CO_2 due to modulation of stomatal opening by phytohormones. In response to altered carbon intake, the changed leaf sugar status acts as a metabolic signal. In concert with other phytohormones, it inhibits growth, which further alters the carbon: nitrogen ratio. The stress conditions generated by severe drought and nutrient deprivation triggers energy imbalances, as well further loop-in alteration between growth promoting and growth retarding phytohormones (Sreenivasulu et al. 2012), generation of reactive oxygen species (ROS) and second messengers such as calcium to affect transcriptional regulation of numerous genes. Their meta-analysis indicated that variables on the time and severity of stress and plant species made it difficult to find a general trend in relating molecular responses to the physiological status of the plant. Functional characterization of stress inducible transcription factors should provide more information in the complex regulatory gene networks that are involved in responses to drought, high temperature, and high salinity stresses. At present, the functions of many of these genes are not fully characterized. Some attempts at analyzing large scale high throughput data allows us to bring the different elements together, suggesting that the integration of stress cues into development and plant growth in dealing with crop yield under stress is rather complicated. Such diversity in needs, approaches, opinions and indeed results has led to generation of massive literature, which needs to be systematically reviewed to derive proper strategies for understanding the stress tolerance mechanisms. Therefore methods implied in systems biology approaches remain pivotal to systematically reveal the function of these stress-responsive pathways.

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