# Functional Genomics and Systems Biology Approach for Understanding Agroecosystems

4

Birendra Singh Yadav and Ashutosh Mani

**Abstract**

Plant metabolism is affected by several biotic and abiotic factors of our environment that leads to low yield in crops. The integrative approach of functional genomics and systems biology is one of the most promising tools for understanding the agroecosystems. In this chapter, we will discuss the role of functional genomics to study the effect of stress on plants. Various approaches and tools of systems biology will be also discussed to understand the alteration in biological networks, i.e., gene regulatory, protein-protein and metabolic networks, etc. Different tools available for studying the agroecosystems using omics and systems biology have been explored here in detail.

## 4.1 Introduction

The natural ecosystems which are modified for the production of food and fiber are known agroecosytems. There are several biotic and abiotic factors that are also present in the natural ecosystems. Agroecosytems supports the production of many crops but the environmental factors affect the productivity of crops (Ptaszek 2013). The interaction of biotic and abiotic stress component of environment affects the life as well productivity of crops, and hence, it is quite necessary to study the role of interference and underlying mechanisms of plants to sustain against the challenges. The agroecosysystems also interact positively and negatively with insects, birds, and weeds and contribute in sustainability of crops (GANS 2005).

Functional genomics is the study of function and interactions of genes/proteins by using genome-wide approaches by integrating the data obtained from different

B. S. Yadav · A. Mani (✉)
Department of Biotechnology, Motilal Nehru National Institute of Technology, Allahabad, India
e-mail: amani@mnnit.ac.in



V. Tripathi et al. (eds.), *Microbial Genomics in Sustainable Agroecosystems*,
https://doi.org/10.1007/978-981-13-8739-5_4

processes like DNA sequence, gene expression, transcriptome profiling, and DNA-protein, RNA-protein, and protein-protein interactions. On the basis of above-mentioned information, one can build the model of interaction that regulates the gene expression and other biological processes (Bunnik and Le Roch 2013). In 1998 Weinstein (Weinstein 1998) coined the term "omics" and classified it into genomics, transcriptomics, and proteomics. Functional genomics fills the research gap between the classical gene expression and genome-wide expression and it is the correlation with biological process (Gasperskaja and Kučinskas 2017).

Plants are ultimate source of energy, food, and other valuable compounds. Systems biology allows us to understand how plants used to synthesize the various valuable compounds as well as it also correlate the phenotype and genotype (Kell 2002; Dhondt et al. 2013). The productivity of various plants is decreasing day by day due to the biotic and abiotic factor of environment, and this includes cold, drought, heat, salinity, and heavy metals (Bebber et al. 2013). Plants are very much susceptible to stresses and sometimes all these stress acts simultaneously and plants act accordingly if they unable to process it may die (Ramegowda and Senthil-Kumar 2015; Mushegian 2017).

Various omics approaches as shown in Fig. 4.1 enable the researcher to identify the stress-responsive genes, pathways, and secondary metabolites using genomics and systems biology tools (Pandey et al. 2015). The integrative approach of transcriptomics, proteomics, metabolomics, phenomics, and interactomics with systems biology is used to understand the underlying mechanism in plants during various stress conditions (Kumar et al. 2015; Ben-Amar et al. 2016; Pandey et al. 2016). The systems of plants are well studied and understood by using the omics and systems biology approach and are useful for discovering the marker genes associated with stress and it is the very first step to develop the tolerance variety of crops (Saito and Matsuda 2010; Dhondt et al. 2013).

In this chapter, we have focused the application of different omics and systems biology approach during biotic and abiotic stress on plants to understand the tolerance strategy of plants.

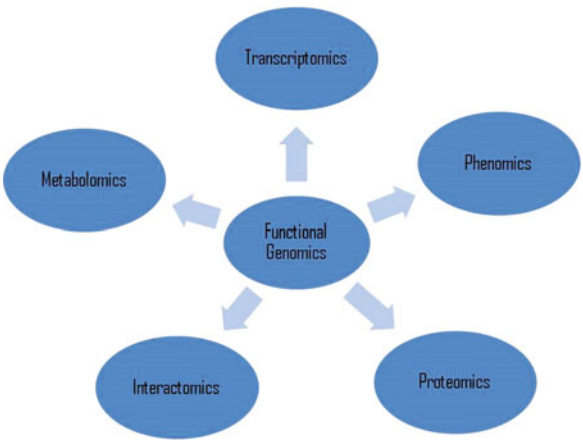


**Fig. 4.1** Various aspects of functional genomics that are used to understand the effect of stress on plants to understand the mechanism of defence

## 4.2 Transcriptomics

Gene expression is also affected by modification in DNA by DNA methylation without changing the DNA sequence. This can be determined by using methylation-dependent restriction enzyme (MDRE) or bisulfite conversion and its PCR (Schuster 2007; Zilberman and Henikoff 2007). Other modifications like acetylation, phosphorylation, and ubiquitination also regulate the gene expression (Bannister and Kouzarides 2011), and it can be investigated using chromatin immunoprecipitation (CHIP) (Shendure and Aiden 2012). The information content of an organism is present in its genomic DNA and is expressed through transcription, where transcriptome requires the information content of genome at a particular time and allow us to study the differential expression pattern at a specific condition (Lowe et al. 2017). The term transcriptome was used in 1990 (Piétu et al. 1999), and before this scientists were using serial analysis of gene expression (SAGE) based on Sanger sequencing (Velculescu et al. 1995).

Next-generation sequencing (NGS) is the massively parallel sequencing of the genome under specific conditions to study the genomes using RNA sequencing (RNA Seq) which is high-throughput sequencing technology (Ozsolak and Milos 2011), and it intakes the RNA in nanogram (Hashimshony et al. 2012). It does not require the prior information of genomic sequencing whose sequencing/analysis has to be done (Stefano 2014) and has high accuracy up to 90% in sequencing. NGS methods are also able to detect the SNPs with high technical reproducibility of 99% (Marioni et al. 2008) as explained in Fig. 4.2 the various aspects of NGS.

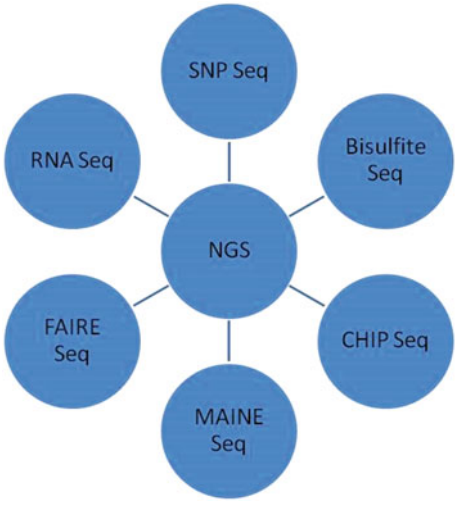


**Fig. 4.2** The various role of Next generation sequencing used for analysis and understanding the biological process in plants and animals

DNA microarray has the ability to measure the simultaneous expression of thousands of genes in at the particular stage of cells (Schena et al. 1995). This technique is used to investigate the diagnostic or prognostic biomarkers, disease-associated genes, and the response of gene against a particular drug/stress in plants and animals to understand the mechanism involved in a particular condition (Aguan et al. 2000; Zhang et al. 2005). The first mRNA is isolated from a normal and experimental condition which are transcribed into cDNA and labeled with dye and finally allowed to hybridize with a probe attached on chip to measure the level of mRNA in control and experimental condition (Gibson and Muse 2009). Lots of studies have been performed on various plants during biotic/abiotic stress using transcriptomics approach, and some important studies are listed in Table 4.1.

**Table 4.1** List of transcriptomics studies available on various plants to understand the abiotic stress using omics approach

| S. No | Species | Stress treatment | Tissue | Comments | References |
|---|---|---|---|---|---|
| 1. | *Arabidopsis thaliana* | Cadmium 5 μM,50 μM | Root and shoot | During cadmium treatment of 50 μM of cd in Arabidopsis, transcriptome study was performed and revealed that the sulfur assimilation pathway was increased leads to more production of GSH and phenylpropanoid biosynthesis was also enhanced | Herbette et al. (2006) |
| 2. | *Glycine max* | Cadmium 40 μM | Root | Oxidative markers production was reduced and free radicals were generated in a large amount and it was also observed that GST was increased during cadmium exposure of 40 μM exposure | McLaughlin et al. (2000) |
| 3. | Barely | Cadmium 80 μM | Roots, shoots | The minimum inhibitory concentration of cadmium was calculated and the treatment of cadmium was given. Exposed roots and shoots were selected and used for mRNA isolation and RNA-Seq was performed but the analysis is not done | Kintlová et al. (2017) |

(continued)

**Table 4.1** (continued)

| S. No | Species | Stress treatment | Tissue | Comments | References |
|---|---|---|---|---|---|
| 4. | *Zea mays* | Cadmium 100 μM | Root | Transcriptome analysis of *Zea mays* was performed under 100 μM of cadmium and it was observed that indole acetic acid (IAA), auxin biosynthesis and transporter genes were underexpressed | Yue et al. (2016) |
| 5. | *Oryza sativa* | Cadmium 50 μM | Root, shoot | Seedlings were damaged and level of expressions of transporter genes was affected, revealed by transcriptome analysis of *Oryza sativa* under exposure of cadmium | Oono et al. (2016) |
| 6. | *Oryza sativa* | Chromium 25 μM, 50 μM, 100 μM, 250 μM | Root | Different concentration of chromium was given to rice and phenotypic studies were performed. Root treated with 100 μM chromium was selected and transcriptome analysis was performed and reported an increased level of lipid peroxidation and proline synthesis. Glutathione plays important role in chromium detoxification as reported by them | Dubey et al. (2010) |
| 7. | *Zea mays* | 300 mg/ml Chromium | Leaves | The chromium stress associated genes were identified and that are responsible for ROS detoxification and defense response. Morphology of *Zea mays* was changed during chromium treatment | Wang et al. (2013) |

(continued)

**Table 4.1** (continued)

| S. No | Species | Stress treatment | Tissue | Comments | References |
|---|---|---|---|---|---|
| 8. | *Brassica napus* | Chromium 25 μM and 100 μM | Leaves | Photosynthesis efficiency, ATP synthesis, and transpiration are adversely affected during exposure of chromium and proteomics study also prove the above-mentioned results. It was also observed that phosphoglycolate production was enhanced during chromium exposure | D'Alessandro et al. (2013) |
| 9. | *Crambe abyssinica* | Chromium 50 μM 100 μM 150 μM 250 μM | Seedlings | Various concentration of chromium is exposed to plant and 150 μM concentration of chromium was selected for further studies. Ion transporter, sulfur assimilation, photosynthesis, photosynthesis, and cell metabolism were affected due to chromium exposure | Zulfiqar et al. (2011) |
| 10. | *Arabidopsis* plant | Arsenic 100 μM 200 μM 300 μM | Root | Different concentration of arsenic was given to tolerance and susceptible varieties of Arabidopsis and he revealed that ethylene-related pathway was changed. Heat shock genes and aqua transporter genes expression was varied | Fu et al. (2014) |
| 11. | Barley | Arsenic 5 μM | Root | Exposure of arsenate and arsenite in barley was compared with other plants and concluded that barely having low uptakes. Phosphate transporter gene was affected and arsenate and arsenite were localized in xylem sap | Su et al. (2010) |

(continued)

**Table 4.1** (continued)

| S. No | Species | Stress treatment | Tissue | Comments | References |
|---|---|---|---|---|---|
| 12. | Maize | Arsenic<br>5 ppm<br>10 ppm | Leaves | Lipid peroxidation was increased due to exposure of arsenate at 10 ppm. SOD and peroxidase activity was also increased during As(V) exposure proved by biochemical assays | Kumar Yadav and Srivastava (2015) |
| 13. | *Crambe abyssinica* | Arsenic<br>100 μM<br>150 μM<br>200 μM<br>250 μM<br>300 μM | Seedlings | For studying molecular mechanism involved for detoxification of as 250 μM concentration exposed to plant and subjected to microarray and reported that sulfur metabolism, heat shock protein, and metal transporter protein expression were altered | Paulose et al. (2010) |
| 14. | *Oryza sativa* | Arsenic<br>5 μM<br>10 μM<br>25 μM<br>50 μM | Root | Root sample treated with 25 μM of as (V) was used to extract the mRNA and microarray was performed. The DEGs involved in cell wall biogenesis and cell cycle were downregulated. The ethylene response factor, heat shock factor, and myb-like genes were upregulated for detoxification of arsenic | Huang et al. (2012) |
| 15. | *Medicago truncatula* | Arsenic<br>25 μM | Root | The microarray of Medicago treated with 25 μM of as(III) was performed and validated with q-RT PCR. Root growth and rate of photosynthesis were decreased | Lafuente et al. (2015) |

It has been revealed by a transcriptomic study that many genes undergo differential exposure during exposure of environmental stress. The genes which are upregulated and downregulated are a key player in several biological processes and molecular function. Stress-responsive gene which is overexpressed is involved in different defense mechanism against the environmental stress while underexpressed genes are generally involved in the storage process. Certain metabolic pathways are overexpressed and underexpressed for providing tolerance against heavy metal stress in chickpea plant (Szklarczyk et al. 2017).

## 4.3 Proteomics

In understanding the biological process, it is necessary to understand the function of the protein in a biological process. Sometimes transcriptomics study does not correlate with proteomics study due to posttranslational modification which changes the function of the protein. Two-dimensional gel electrophoresis can be used to analyze the protein content on a cell where proteins are first separated by size followed by mass spectrometry. LC-MS is also one of the approaches where proteins are first separated by one-dimensional SDS PAGE, then protein is digested and separated by LC and analyzed by MS. Multidimensional protein identification technology is high-throughput technology used for separating protein from complex mixture by digesting proteins into peptides followed by separation on the basis of charge and hydrophobicity and finally analyzed by MS. (Washburn et al. 2001). The signal obtained from MS data is compared with a database for identification of the protein.

Stress associated proteins were differentially expressed during abiotic stress as reported in various literature contributing towards the stress tolerance (Witzel et al. 2009; Hossain et al. 2012; Pérez-Clemente et al. 2013). The different proteomic study has been performed for, e.g., drought stress (Caruso et al. 2008; Mirzaei et al. 2012; Mohammadi et al. 2012; Cramer et al. 2013; Zhang et al. 2016), salt stress (Nam et al. 2012; Zhu et al. 2012), water lodging (Komatsu et al. 2009, 2010, 2013a, b, 2014, Alam et al. 2010a, b), and heat stress (Rollins et al. 2013; Xuan et al. 2013). The complex biological process is analyzed using proteomics in plants during stress (Aghaei and Komatsu 2013; Ghosh and Xu 2014; Gong et al. 2015). The methodology of the proteomics approach for identifying candidate protein during stress condition is shown in Fig. 4.3.

## 4.4 Interactomics

The union of informatics, biochemistry, and engineering technology enables the researcher to understand the interactions of proteins used to study under interactomics. The omics technology enable the researcher to understand the biological system and interaction of expressed proteins in a cell (the proteome) and genome encoded product along with its interaction in complex biological

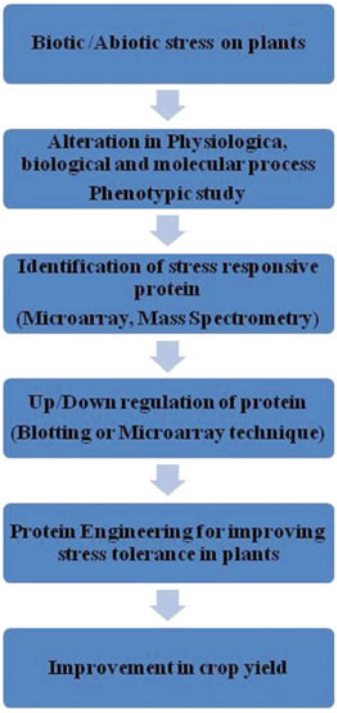


**Fig. 4.3** Flow chart of methodology to perform the proteomics study on plants during stress conditions

network i.e. the interactome. It is a fast-growing area of systems biology for understanding the biological process and regulatory network during biotic and abiotic stress in plants. The study of interactions in signal transduction, transcriptional regulation, metabolic pathways, and other biological processes is said as interactomics. Lots of approaches have been developed for studying the interactome like in silico, in vivo, and in vitro (Rao et al. 2014). The first approach includes the computational analysis and text mining; in vivo includes Y2H hybrid system, while the in vitro method experiments are performed on the living organism to understand the biological functions interactome.

Uhrig, Williams, and Bowles in 2006 performed the protein-protein interaction network study on Arabidopsis that was based on literature mining and co-expression approach (Williams and Bowles 2004; Uhrig 2006). Jane Geisler-Lee in 2007, predicted Arabidopsis protein interactome based on the interolog method. They also concluded that the predicted proteins were co-localized and co-expressed by analyzing existing experimental data from Arabidopsis and decipher the significant role of signaling and cellular function by enabling hypothesis generation Arabidopsis interactome (Geisler-Lee et al. 2007).

## 4.5 Metabolomics

The study of metabolites at the particular instant in agroecosystem is known as metabolomics. It is important to understand the plant stress response in terms of metabolites. Lots of studies have been done for deciphering the role of metabolite during different abiotic stress condition. In 2004, Rizhky performed the metabolic profiling of plants during drought, heat, and combined stress and reported accumulation of sucrose and other sugar like starch (Rizhsky 2004). NMR based metabolic fingerprinting of plants during heavy metal stress were performed by Bailey in 2003 and responsible metabolic pathways were explored (Bailey et al. 2003). The microarray data of chickpea during heavy metal stress were analyzed and responsible pathways which were providing tolerance were also identified. It was seen that Nitrogen metabolism, Starch sucrose metabolism, and Riboflavin metabolism were altered. Several metabolomics approacheses was also used to understand the production of metabolite during different stress condition in plants like water salinity (Cramer et al. 2007), oxidative stress (Baxter et al. 2006), and heavy metal stress (Le Lay et al. 2006).

The metabolomics data is similar to transcriptomics and proteomics data. It requires lots of computational work including file handling, data mining, and finally comparative analysis. Lots of online server/databases/tools are available for analysis and visualization of metabolic pathway for understanding the agroecosystem shown in Table 4.2. Once the function of metabolite will be known, one can directly correlate with the function of the gene during particular stress condition. It is a rapidly growing technology to understand the metabolic pathways in plants by using different strategies like targeted analysis, metabolite profiling, and metabolic fingerprinting (Fiehn 2002; Halket et al. 2005; Shulaev 2006).

**Table 4.2** List of various online tools and their web address that are used for analysis of various metabolic pathways in plants

| Pathway database/ tools | Web address | References |
|---|---|---|
| KEGG | https://www.genome.jp/kegg/ | Kanehisa et al. (2017) |
| BioCyc | https://biocyc.org/ | Paley and Karp (2006) |
| MetaCyc | https://metacyc.org/ | Caspi (2006) |
| AraCyc | https://www.plantcyc.org/databases/aracyc/15.0 | Zhang (2005) |
| MapMan | https://mapman.gabipd.org/ | Thimm et al. (2004) |
| KaPPA-view | http://kpv.kazusa.or.jp/ | Tokimatsu (2005) |
| BioPathAT | http://www.murdockmetabolomics.wsu.edu/LangeLabHome.html | Lange and Ghassemian (2005) |
| MetNetDB | http://metnetweb.gdcb.iastate.edu/MetNet_db.htm | Wurtele et al. (2003) |

## 4.6 Phenomics

Generally, plants interact with the biotic and abiotic component of the ecosystem. As a result, there is a change in genotype and phenotype of plants. The alteration in phenotype is due to combined interaction of genome with the environment. The study of phenotype during the interaction of biotic and abiotic factor of the environment at a particular instant is known as phenomics. Invasive and noninvasive techniques are available to understand the change in phenotype in model plants (Großkinsky et al. 2015). Phenomics technology is used in basic plant research during different stress conditions and crop breeding (Furbank and Tester 2011). A noninvasive method of plant phenomics methodology is shown in Fig. 4.4.

In image acquisition, digital image of plants is taken to study the effect of biotic and abiotic effect on plants. It is done by several approaches like tomography imaging (Bovik 2005), thermography imaging (Padhi et al. 2012), LIDAR (Lenco 1982), and time-of-flight camera (Klose et al. 2011). After image acquisition, processing of the image is done for removing the noise and improving the contrast (Hamuda et al. 2016). Image cropping, contrast improvement, and dimensional reduction are major operation done during image processing (Singh et al. 2016). After the image preprocessing, segmentation of image is done, in which objects are identified and isolated by removing irrelevant background present in the objects (Singh and Misra 2017). In the feature extraction process, the image of interest is used to extract the numerical value where different algorithms can be applied to understand the phenotype (Van Der Heijden et al. 2012). Finally, the generated data is analyzed by a machine-learning approach (Ghatak 2017).

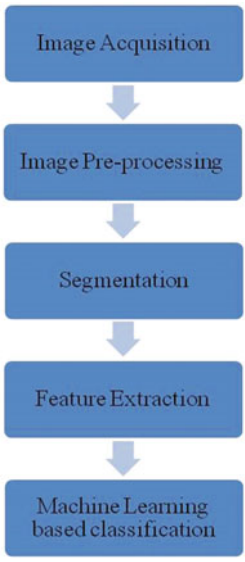


**Fig. 4.4** Various steps involved in generation and analysis of Phenomics data in plants for understanding the effect of stress

## 4.7 Role of Systems Biology for Understanding Agroecosystem

For a comprehensive study of plants systems biology, the role of bioinformatics is crucial. "Omics" data analysis and interpretation required the good skill of bioinformatics and algorithm (Joyce and Palsson 2006). The omics data can be analyzed for understanding plants systems, and this requires lots of tools for visualization of networks and construction of pathways and analysis tools as shown in Fig. 4.5.

Systems biology represents the graphical view of biomolecules and their interactions in the form of a biological network (BN). In BN, nodes of the graph represent the gene/protein/DNA/RNA and edges represent the way of interaction. The interaction may be direct (flow of information from one to another biomolecule) and undirected (having interaction but the direction is not sure). The way of interaction may be physical interaction, metabolic reaction, and regulatory connection (Joyce and Palsson 2006). The most connected node in networks is termed as hub node, which is a key player in BN (Barabási and Oltvai 2004). During stress condition in plants, the interaction between biomolecule changes and it can be well studied and understood by using systems biology by constructing or reconstructing gene to metabolite network, protein-protein interaction networks, gene regulatory networks, and transcriptional regulatory network (Yuan et al. 2008).

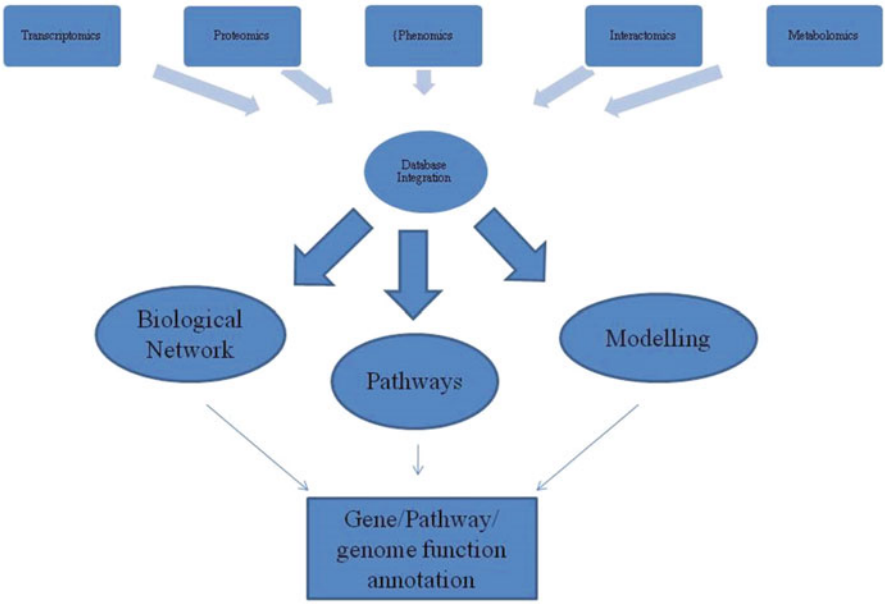


**Fig. 4.5** Integrative approach using omics and systems biology to understand the plants system during stress conditions

## 4.8 Gene to Metabolite Networks

Gene to metabolite networks is made on the basis of the coefficient of correlation between genes. The way of interaction is represented on the basis of the correlation value. A different biological process, molecular functions, and gene functions can be explored to understand plants systems biology during normal and experimental conditions. Various studies on different plants have been performed to understand the gene to metabolite network and candidate gene responsible for over- or under-production of secondary metabolites were identified during stress and normal conditions (Goossens 2003; Scheible 2004; Zulak et al. 2007).

## 4.9 Protein-Protein Interaction Networks

In PPI networks, nodes are represented by the proteins and edges represents the physical or genetic interaction. The function of genes is explored on the basis of genetic interaction between the proteins (Boone et al. 2007) while physical interactions are used to understand protein-protein interaction and dimer formation (de Folter 2005). Analysis on the basis of biological networks construction in chickpea during cadmium and chromium exposure has been reported that most of the hub genes are involved in protein dimerization (Yadav and Mani 2018).

## 4.10 Transcriptional Regulatory Networks

Interaction of the transcription factor and downstream gene are studied in this type of networks. Here nodes are transcription factor or regulatory genes and represent the activation and deactivation (Babu et al. 2004). One transcription factor interacts with a large number of genes simultaneously. Different studies have been performed to understand the stress response in plants using transcriptional regulatory networks (Nakashima et al. 2009; Yun et al. 2010; Todaka et al. 2012).

## 4.11 Gene Regulatory Networks

In gene regulatory networks, node represents the genes/mRNA/proteins and edges are regulatory interaction like activation, repression, inhibition, or functional interactions (Long et al. 2008). Various studies reported that gene regulatory network having an important role to understand the underlying mechanisms during developmental and stress condition on the basis of gene regulatory network in different plants (Li et al. 2006; Meng et al. 2011; Pires et al. 2013). There are lots of tools available for construction and analysis of biological network in plants which are shown in Table 4.3.

**Table 4.3** List of frequently used software and online tools used for construction of biological networks and their analysis using genomics data in plants

| Software/tools | Description | Reference |
|---|---|---|
| Cytoscape | It is widely used software to construct, visualize, and analyze the biological network | Shannon, et al. (2003) |
| Genemania | It is an online tool for construction and analysis of biological network | Franz et al. (2018) |
| Cell designer | A software for analyzing the biological network | Funahashi et al. (2006) |
| Networks | Software used for biological network analysis | Team (2014) |
| Medusa | Software used for visualization of small network | Bosi et al. (2015) |
| BioLayout Express3D | A tool for biological network visualization and analysis | Wright et al. (2014) |
| String | An online tool for construction and visualization of a biological network | Szklarczyk et al. (2017) |

## 4.12 Conclusion

In upcoming years, plants will be a solution of all problems like water and food scarcity. So, it is very important to understand the agroecosystem; for this one should know about functional genomics and systems biology. The functional genomics and systems biology can be used to develop a strategy to escape the plants from stress condition and new variety can also be developed. In addition to advantage, there are certain challenges like big data handling and its analysis. Due to the complexity of plants, wet lab experiment is not always possible; hence there is a need of lots of computational approaches that can be applied to functional genomics and systems biology to understand the agroecosystem in a well-defined manner.

## References

Aghaei K, Komatsu S (2013) Crop and medicinal plants proteomics in response to salt stress. Front Plant Sci 4. https://doi.org/10.3389/fpls.2013.00008

Aguan K, Carvajal JA, Thompson LP, Weiner CP (2000) Application of a functional genomics approach to identify differentially expressed genes in human myometrium during pregnancy and labour. Mol Hum Reprod 6:1141–1145

Alam I, Lee DG, Kim KH et al (2010a) Proteome analysis of soybean roots under waterlogging stress at an early vegetative stage. J Biosci 35:49–62. https://doi.org/10.1007/s12038-010-0007-5

Alam I, Sharmin SA, Kim KH et al (2010b) Proteome analysis of soybean roots subjected to short-term drought stress. Plant Soil 333:491–505. https://doi.org/10.1007/s11104-010-0365-7

Babu MM, Luscombe NM, Aravind L et al (2004) Structure and evolution of transcriptional regulatory networks. Curr Opin Struct Biol 14:283–291

Bailey NJC, Oven M, Holmes E et al (2003) Metabolomic analysis of the consequences of cadmium exposure in Silene cucubalus cell cultures via 1H NMR spectroscopy and chemometrics. Phytochemistry 62:851–858. https://doi.org/10.1016/S0031-9422(02)00719-7

Bannister AJ, Kouzarides T (2011) Regulation of chromatin by histone modifications. Cell Res 21:381–395. https://doi.org/10.1038/cr.2011.22

Barabási AL, Oltvai ZN (2004) Network biology: understanding the cell's functional organization. Nat Rev Genet 5:101–113

Baxter CJ, Redestig H, Schauer N et al (2006) The metabolic response of heterotrophic Arabidopsis cells to oxidative stress. Plant Physiol 143:312–325. https://doi.org/10.1104/pp.106.090431

Bebber DP, Ramotowski MAT, Gurr SJ (2013) Crop pests and pathogens move polewards in a warming world. Nat Clim Chang 3:985–988. https://doi.org/10.1038/nclimate1990

Ben-Amar A, Daldoul S, Reustle GM et al (2016) Reverse genetics and high throughput sequencing methodologies for plant functional genomics. Curr Genomics 17:460–475. https://doi.org/10.2174/1389202917666160520102827

Boone C, Bussey H, Andrews BJ (2007) Exploring genetic interactions and networks with yeast. Nat Rev Genet 8:437–449

Bosi E, Donati B, Galardini M et al (2015) MeDuSa: a multi-draft based scaffolder. Bioinformatics 31:2443–2451. https://doi.org/10.1093/bioinformatics/btv171

Bovik A (2005) Handbook of image and video processing

Bunnik EM, Le Roch KG (2013) An introduction to functional genomics and systems biology. Adv Wound Care 2:490–498. https://doi.org/10.1089/wound.2012.0379

Caruso G, Cavaliere C, Guarino C et al (2008) Identification of changes in Triticum durum L. leaf proteome in response to salt stress by two-dimensional electrophoresis and MALDI-TOF mass spectrometry. Anal Bioanal Chem 391:381–390. https://doi.org/10.1007/s00216-008-2008-x

Caspi R (2006) MetaCyc: a multiorganism database of metabolic pathways and enzymes. Nucleic Acids Res 34:D511–D516. https://doi.org/10.1093/nar/gkj128

Cramer GR, Ergül A, Grimplet J et al (2007) Water and salinity stress in grapevines: early and late changes in transcript and metabolite profiles. Funct Integr Genomics 7:111–134. https://doi.org/10.1007/s10142-006-0039-y

Cramer GR, Van Sluyter SC, Hopper DW et al (2013) Proteomic analysis indicates massive changes in metabolism prior to the inhibition of growth and photosynthesis of grapevine (Vitis vinifera L.) in response to water deficit. BMC Plant Biol 13. https://doi.org/10.1186/1471-2229-13-49

D'Alessandro A, Taamalli M, Gevi F et al (2013) Cadmium stress responses in Brassica juncea: hints from proteomics and metabolomics. J Proteome Res 12:4979–4997. https://doi.org/10.1021/pr400793e

de Folter S (2005) Comprehensive interaction map of the Arabidopsis MADS box transcription factors. Plant Cell Online 17:1424–1433. https://doi.org/10.1105/tpc.105.031831

Dhondt S, Wuyts N, Inzé D (2013) Cell to whole-plant phenotyping: the best is yet to come. Trends Plant Sci 18:1360–1385

Dubey S, Misra P, Dwivedi S et al (2010) Transcriptomic and metabolomic shifts in rice roots in response to Cr (VI) stress. BMC Genomics 11. https://doi.org/10.1186/1471-2164-11-648

Fiehn O (2002) Metabolomics – the link between genotypes and phenotypes. Plant Mol Biol 48:155–171. https://doi.org/10.1023/A:1013713905833

Franz M, Rodriguez H, Lopes C et al (2018) GeneMANIA update 2018. Nucleic Acids Res 46:W60–W64. https://doi.org/10.1093/nar/gky311

Fu S-F, Chen P-Y, Nguyen QTT et al (2014) Transcriptome profiling of genes and pathways associated with arsenic toxicity and tolerance in Arabidopsis. BMC Plant Biol 14:94. https://doi.org/10.1186/1471-2229-14-94

Funahashi A, Matsuoka Y, Jouraku A, et al (2006) Celldesigner: a modeling tool for biochemical networks. In: Proceedings – Winter Simulation Conference. pp 1707–1712

Furbank RT, Tester M (2011) Phenomics - technologies to relieve the phenotyping bottleneck. Trends Plant Sci 16:635–644

Gans C (2005) Checklist and bibliography of the amphisbaenia of the world. Bull Am Museum Nat Hist 289:1. https://doi.org/10.1206/0003-0090(2005)289<0001:CABOTA>2.0.CO;2

Gasperskaja E, Kučinskas V (2017) The most common technologies and tools for functional genome analysis. Acta medica Litu 24:1–11. https://doi.org/10.6001/actamedica.v24i1.3457
Geisler-Lee J, O'Toole N, Ammar R et al (2007) A predicted Interactome for Arabidopsis. Plant Physiol 145:317–329. https://doi.org/10.1104/pp.107.103465
Ghatak A (2017) Machine learning with R. Springer, Singapore
Ghosh D, Xu J (2014) Abiotic stress responses in plant roots: a proteomics perspective. Front Plant Sci 5. https://doi.org/10.3389/fpls.2014.00006
Gibson G, Muse SV (2009) Primer of genome science. Sinauer Associates, Sunderland
Gong F, Hu X, Wang W (2015) Proteomic analysis of crop plants under abiotic stress conditions: where to focus our research? Front Plant Sci 6. https://doi.org/10.3389/fpls.2015.00418
Goossens A (2003) Secretion of secondary metabolites by ATP-binding cassette transporters in plant cell suspension cultures. Plant Physiol 131:1161–1164. https://doi.org/10.1104/pp.102.016329
Großkinsky DK, Svensgaard J, Christensen S, Roitsch T (2015) Plant phenomics and the need for physiological phenotyping across scales to narrow the genotype-to-phenotype knowledge gap. J Exp Bot 66:5429–5440
Halket JM, Waterman D, Przyborowska AM, et al (2005) Chemical derivatization and mass spectral libraries in metabolic profiling by GC/MS and LC/MS/MS. In: J Exp Botany 56(410). pp 219–243
Hamuda E, Glavin M, Jones E (2016) A survey of image processing techniques for plant extraction and segmentation in the field. Comput Electron Agric 125:184–199
Hashimshony T, Wagner F, Sher N, Yanai I (2012) CEL-Seq: single-cell RNA-Seq by multiplexed linear amplification. Cell Rep 2:666–673. https://doi.org/10.1016/j.celrep.2012.08.003
Herbette S, Taconnat L, Hugouvieux V et al (2006) Genome-wide transcriptome profiling of the early cadmium response of Arabidopsis roots and shoots. Biochimie 88:1751–1765. https://doi.org/10.1016/j.biochi.2006.04.018
Hossain Z, Nouri MZ, Komatsu S (2012) Plant cell organelle proteomics in response to abiotic stress. J Proteome Res 11:37–48
Huang T-L, Nguyen QTT, Fu S-F et al (2012) Transcriptomic changes and signalling pathways induced by arsenic stress in rice roots. Plant Mol Biol 80:587–608. https://doi.org/10.1007/s11103-012-9969-z
Joyce AR, Palsson BØ (2006) The model organism as a system: integrating "omics" data sets. Nat Rev Mol Cell Biol 7:198–210
Kanehisa M, Furumichi M, Tanabe M et al (2017) KEGG: new perspectives on genomes, pathways, diseases and drugs. Nucleic Acids Res 45:D353–D361. https://doi.org/10.1093/nar/gkw1092
Kell DB (2002) Genotype - phenotype mapping: genes as computer programs. Trends Genet 18:555–559
Kintlová M, Blavet N, Cegan R, Hobza R (2017) Transcriptome of barley under three different heavy metal stress reaction. Genomics Data 13:15–17. https://doi.org/10.1016/j.gdata.2017.05.016
Klose R, Penlington J, Ruckelshausen A (2011) Usability of 3D time-of-flight cameras for automatic plant phenotyping. Bornimer Agrartech Berichte 69:93–105. https://doi.org/10.1103/PhysRevC.92.024618
Komatsu S, Yamada E, Furukawa K (2009) Cold stress changes the concanavalin A-positive glycosylation pattern of proteins expressed in the basal parts of rice leaf sheaths. Amino Acids 36:115–123. https://doi.org/10.1007/s00726-008-0039-4
Komatsu S, Sugimoto T, Hoshino T et al (2010) Identification of flooding stress responsible cascades in root and hypocotyl of soybean using proteome analysis. Amino Acids 38:729–738. https://doi.org/10.1007/s00726-009-0277-0
Komatsu S, Makino T, Yasue H (2013a) Proteomic and biochemical analyses of the cotyledon and root of flooding-stressed soybean plants. PLoS One 8(6). https://doi.org/10.1371/journal.pone.0065301

Komatsu S, Nanjo Y, Nishimura M (2013b) Proteomic analysis of the flooding tolerance mechanism in mutant soybean. J Proteome 79:231–250. https://doi.org/10.1016/j.jprot.2012.12.023

Komatsu S, Nakamura T, Sugimoto Y, Sakamoto K (2014) Proteomic and Metabolomic analyses of soybean root tips under flooding stress. Protein Pept Lett 21:865–884. https://doi.org/10.2174/0929866521666140320110521

Kumar Yadav R, Srivastava SK (2015) Effect of Arsenite and arsenate on lipid peroxidation, Enzymatic and Non-Enzymatic Antioxidants in Zea mays Linn Biochem Physiol Open Access 4:. https://doi.org/10.4172/2168-9652.1000186

Kumar D, Chapagai D, Dean P, Davenport M (2015) Biotic and abiotic stress signaling mediated by salicylic acid. In: Elucidation of abiotic stress signaling in plants: functional genomics perspectives. pp 329–346

Lafuente A, Pérez-Palacios P, Doukkali B et al (2015) Unraveling the effect of arsenic on the model Medicago-Ensifer interaction: a transcriptomic meta-analysis. New Phytol 205:255–272. https://doi.org/10.1111/nph.13009

Lange BM, Ghassemian M (2005) Comprehensive post-genomic data analysis approaches integrating biochemical pathway maps. Phytochemistry 66:413–451

Le Lay P, Isaure MP, Sarry JE et al (2006) Metabolomic, proteomic and biophysical analyses of Arabidopsis thaliana cells exposed to a caesium stress. Influence Potassium Supply Biochimie 88:1533–1547. https://doi.org/10.1016/j.biochi.2006.03.013

Lenco M (1982) Remote sensing and natural resources. Nat Resour 18:2–9

Li S, Assmann SM, Albert R (2006) Predicting essential components of signal transduction networks: a dynamic model of guard cell abscisic acid signaling. PLoS Biol 4:1732–1748. https://doi.org/10.1371/journal.pbio.0040312

Long TA, Brady SM, Benfey PN (2008) Systems approaches to identifying gene regulatory networks in plants. Annu Rev Cell Dev Biol 24:81–103. https://doi.org/10.1146/annurev.cellbio.24.110707.175408

Lowe R, Shirley N, Bleackley M et al (2017) Transcriptomics technologies. PLoS Comput Biol 13. https://doi.org/10.1371/journal.pcbi.1005457

Marioni JC, Mason CE, Mane SM et al (2008) RNA-seq: an assessment of technical reproducibility and comparison with gene expression arrays. Genome Res 18:1509–1517. https://doi.org/10.1101/gr.079558.108

McLaughlin MJ, Zarcinas BA, Stevens DP, Cook N (2000) Soil testing for heavy metals. Commun Soil Sci Plant Anal 31:1661–1700. https://doi.org/10.1080/00103620009370531

Meng Y, Shao C, Wang H, Chen M (2011) The regulatory activities of plant MicroRNAs: a more dynamic perspective. Plant Physiol 157:1583–1595. https://doi.org/10.1104/pp.111.187088

Mirzaei M, Soltani N, Sarhadi E et al (2012) Shotgun proteomic analysis of long-distance drought signaling in rice roots. J Proteome Res 11:348–358. https://doi.org/10.1021/pr2008779

Mohammadi PP, Moieni A, Hiraga S, Komatsu S (2012) Organ-specific proteomic analysis of drought-stressed soybean seedlings. J Proteome 75:1906–1923. https://doi.org/10.1016/j.jprot.2011.12.041

Mushegian AA (2017) Stress signals in plants. Sci Signal 10

Nakashima K, Ito Y, Yamaguchi-Shinozaki K (2009) Transcriptional regulatory networks in response to abiotic stresses in Arabidopsis and grasses. Plant Physiol 149:88–95. https://doi.org/10.1104/pp.108.129791

Nam MH, Huh SM, Kim KM et al (2012) Comparative proteomic analysis of early salt stress-responsive proteins in roots of SnRK2 transgenic rice. Proteome Sci 10. https://doi.org/10.1186/1477-5956-10-25

Oono Y, Yazawa T, Kanamori H et al (2016) Genome-wide transcriptome analysis of cadmium stress in rice. Biomed Res Int 2016. https://doi.org/10.1155/2016/9739505

Ozsolak F, Milos PM (2011) RNA sequencing: advances, challenges and opportunities. Nat Rev Genet 12:87–98. https://doi.org/10.1038/nrg2934

Padhi J, Misra RK, Payero JO (2012) Estimation of soil water deficit in an irrigated cotton field with infrared thermography. F Crop Res 126:45–55. https://doi.org/10.1016/j.fcr.2011.09.015

Paley SM, Karp PD (2006) The pathway tools cellular overview diagram and Omics viewer. Nucleic Acids Res 34:3771–3778. https://doi.org/10.1093/nar/gkl334
Pandey A, Sharma M, Pandey GK (2015) Small and large G proteins in biotic and abiotic stress responses in plants. In: Elucidation of abiotic stress signaling in plants: functional genomics perspectives. pp 231–270
Pandey GK, Pandey A, Prasad M, Böhmer M (2016) Editorial: abiotic stress signaling in plants: functional genomic intervention. Front Plant Sci 7. https://doi.org/10.3389/fpls.2016.00681
Paulose B, Kandasamy S, Dhankher OP (2010) Expression profiling of Crambe abyssinica under arsenate stress identifies genes and gene networks involved in arsenic metabolism and detoxification. BMC Plant Biol 10. https://doi.org/10.1186/1471-2229-10-108
Pérez-Clemente RM, Vives V, Zandalinas SI et al (2013) Biotechnological approaches to study plant responses to stress. Biomed Res Int 2013
Piétu G, Mariage-Samson R, Fayein NA et al (1999) The genexpress IMAGE knowledge base of the human brain transcriptome: a prototype integrated resource for functional and computational genomics. Genome Res 9:195–209. https://doi.org/10.1101/gr.9.2.195
Pires ND, Yi K, Breuninger H et al (2013) Recruitment and remodeling of an ancient gene regulatory network during land plant evolution. Proc Natl Acad Sci 110:9571–9576. https://doi.org/10.1073/pnas.1305457110
Ptaszek M (2013) Progress in molecular biology and translational science. In: Progress in molecular biology and translational science. pp 59–108
Ramegowda V, Senthil-Kumar M (2015) The interactive effects of simultaneous biotic and abiotic stresses on plants: mechanistic understanding from drought and pathogen combination. J Plant Physiol 176:47–54
Rao VS, Srinivas K, Sujini GN, Kumar GNS (2014) Protein-protein interaction detection: methods and analysis. Int J Proteomics 2014:1–12. https://doi.org/10.1155/2014/147648
Rizhsky L (2004) When defense pathways collide. The response of Arabidopsis to a combination of drought and heat stress. Plant Physiol 134:1683–1696. https://doi.org/10.1104/pp.103.033431
Rollins JA, Habte E, Templer SE et al (2013) Leaf proteome alterations in the context of physiological and morphological responses to drought and heat stress in barley (Hordeum vulgare L.). J Exp Bot 64:3201–3212. https://doi.org/10.1093/jxb/ert158
Saito K, Matsuda F (2010) Metabolomics for functional genomics, systems biology, and biotechnology. Annu Rev Plant Biol 61:463–489. https://doi.org/10.1146/annurev.arplant.043008.092035
Scheible W-R (2004) Genome-wide reprogramming of primary and secondary metabolism, protein synthesis, cellular growth processes, and the regulatory infrastructure of Arabidopsis in response to nitrogen. Plant Physiol 136:2483–2499. https://doi.org/10.1104/pp.104.047019
Schena M, Shalon D, Davis RW, Brown PO (1995) Quantitative monitoring of gene expression patterns with a complementary DNA microarray. Science 270:467–470. https://doi.org/10.1126/science.270.5235.467
Schuster SC (2007) Next-generation sequencing transforms today's biology. Nat Methods 5:16–18. https://doi.org/10.1038/nmeth1156
Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, Amin N, Schwikowski BIT (2003) Cytoscape: an open source platform for complex network analysis and visualization. Genome Res. http://www.cytoscape.org/
Shendure J, Aiden EL (2012) The expanding scope of DNA sequencing. Nat Biotechnol 30:1084–1094. https://doi.org/10.1038/nbt.2421
Shulaev V (2006) Metabolomics technology and bioinformatics. Brief Bioinform 7:128–139
Singh V, Misra AK (2017) Detection of plant leaf diseases using image segmentation and soft computing techniques. Inf Process Agric 4:41–49. https://doi.org/10.1016/j.inpa.2016.10.005
Singh A, Ganapathysubramanian B, Singh AK, Sarkar S (2016) Machine learning for high-throughput stress phenotyping in plants. Trends Plant Sci 21:110–124
Stefano GB (2014) Comparing Bioinformatic gene expression profiling methods: microarray and RNA-Seq. Med Sci Monit Basic Res 20:138–142. https://doi.org/10.12659/MSMBR.892101

Su YH, McGrath SP, Zhao FJ (2010) Rice is more efficient in arsenite uptake and translocation than wheat and barley. Plant Soil 328:27–34. https://doi.org/10.1007/s11104-009-0074-2

Szklarczyk D, Morris JH, Cook H et al (2017) The STRING database in 2017: quality-controlled protein-protein association networks, made broadly accessible. Nucleic Acids Res 45:D362–D368. https://doi.org/10.1093/nar/gkw937

Team N (2014) NetworkX. networkx.github.io

Thimm O, Bläsing O, Gibon Y et al (2004) MAPMAN: a user-driven tool to display genomics data sets onto diagrams of metabolic pathways and other biological processes. Plant J 37:914–939. https://doi.org/10.1111/j.1365-313X.2004.02016.x

Todaka D, Nakashima K, Shinozaki K, Yamaguchi-Shinozaki K (2012) Toward understanding transcriptional regulatory networks in abiotic stress responses and tolerance in rice. Rice 5:1–9

Tokimatsu T (2005) KaPPA-view. A web-based analysis tool for integration of transcript and metabolite data on plant metabolic pathway maps. Plant Physiol 138:1289–1300. https://doi.org/10.1104/pp.105.060525

Uhrig JF (2006) Protein interaction networks in plants. Planta 224:771–781

Van Der Heijden G, Song Y, Horgan G et al (2012) SPICY: towards automated phenotyping of large pepper plants in the greenhouse. Funct Plant Biol 39:870–877. https://doi.org/10.1071/FP12019

Velculescu VE, Zhang L, Vogelstein B, Kinzler KW (1995) Serial analysis of gene expression. Science 270:484–487. https://doi.org/10.1126/science.270.5235.484

Wang R, Gao F, Guo BQ et al (2013) Short-term chromium-stress-induced alterations in the maize leaf proteome. Int J Mol Sci 14:11125–11144. https://doi.org/10.3390/ijms140611125

Washburn MP, Wolters D, Yates JR (2001) Large-scale analysis of the yeast proteome by multidimensional protein identification technology. Nat Biotechnol 19:242–247. https://doi.org/10.1038/85686

Weinstein JN (1998) Fishing expeditions. Science 282:627

Williams EJB, Bowles DJ (2004) Coexpression of neighboring genes in the genome of Arabidopsis thaliana. Genome Res 14:1060–1067. https://doi.org/10.1101/gr.2131104

Witzel K, Weidner A, Surabhi GK et al (2009) Salt stress-induced alterations in the root proteome of barley genotypes with contrasting response towards salinity. J Exp Bot 60:3545–3557. https://doi.org/10.1093/jxb/erp198

Wright DW, Angus T, Enright AJ, Freeman TC (2014) Visualisation of BioPAX networks using BioLayout Express3D. F1000Research. https://doi.org/10.12688/f1000research.5499.1

Wurtele ES, Li J, Diao L et al (2003) MetNet: software to build and model the biogenetic lattice of Arabidopsis. Comp Funct Genomics 4:239–245. https://doi.org/10.1002/cfg.285

Xuan J, Song Y, Zhang H et al (2013) Comparative proteomic analysis of the stolon cold stress response between the C4 perennial grass species Zoysia japonica and Zoysia metrella. PLoS One 8. https://doi.org/10.1371/journal.pone.0075705

Yadav BS, Mani A (2018) Analysis of bHLH coding genes of Cicer arietinum during heavy metal stress using biological network. Physiol Mol Biol Plants. https://doi.org/10.1007/s12298-018-0625-1

Yuan JS, Galbraith DW, Dai SY et al (2008) Plant systems biology comes of age. Trends Plant Sci 13:165–171

Yue R, Lu C, Qi J et al (2016) Transcriptome analysis of cadmium-treated roots in maize (Zea mays L.). Front Plant Sci 7. https://doi.org/10.3389/fpls.2016.01298

Yun KY, Park MR, Mohanty B et al (2010) Transcriptional regulatory network triggered by oxidative signals configures the early response mechanisms of japonica rice to chilling stress. BMC Plant Biol 10. https://doi.org/10.1186/1471-2229-10-16

Zhang P (2005) MetaCyc and AraCyc. Metabolic pathway databases for plant research. Plant Physiol 138:27–37. https://doi.org/10.1104/pp.105.060376

Zhang X, Jafari N, Barnes RB et al (2005) Studies of gene expression in human cumulus cells indicate pentraxin 3 as a possible marker for oocyte quality. Fertil Steril 83:1169–1179. https://doi.org/10.1016/j.fertnstert.2004.11.030

Zhang H, Ni Z, Chen Q et al (2016) Proteomic responses of drought-tolerant and drought-sensitive cotton varieties to drought stress. Mol Gen Genomics 291:1293–1303. https://doi.org/10.1007/s00438-016-1188-x

Zhu Z, Chen J, Zheng HL (2012) Physiological and proteomic characterization of salt tolerance in a mangrove plant, Bruguiera gymnorrhiza (L.) Lam. Tree Physiol 32:1378–1388. https://doi.org/10.1093/treephys/tps097

Zilberman D, Henikoff S (2007) Genome-wide analysis of DNA methylation patterns. Development 134:3959–3965. https://doi.org/10.1242/dev.001131

Zulak KG, Cornish A, Daskalchuk TE et al (2007) Gene transcript and metabolite profiling of elicitor-induced opium poppy cell cultures reveals the coordinate regulation of primary and secondary metabolism. Planta 225:1085–1106. https://doi.org/10.1007/s00425-006-0419-5

Zulfiqar A, Paulose B, Chhikara S, Dhankher OP (2011) Identifying genes and gene networks involved in chromium metabolism and detoxification in Crambe abyssinica. Environ Pollut 159:3123–3128. https://doi.org/10.1016/j.envpol.2011.06.027