Plant Biotechnology 34, 165–172 (2017)
DOI: 10.5511/plantbiotechnology.17.0619a

Note

Gene coexpression network for *trans*-1,4-polyisoprene biosynthesis involving mevalonate and methylerythritol phosphate pathways in *Eucommia ulmoides* Oliver

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Received December 22, 2016; accepted June 19, 2017 (Edited by K. Aoki)

Abstract *Eucommia ulmoides*, a deciduous dioecious plant species, accumulates *trans*-1,4-polyisoprene (TPI) in its tissues such as pericarp and leaf. Probable TPI synthase (*trans*-isoprenyl diphosphate synthase (*TIDS*)) genes were identified by expressed sequence tags of this species; however, the metabolic pathway of TPI biosynthesis, including the role of *TIDS*s, is unknown. To understand the mechanism of TPI biosynthesis at the transcriptional level, comprehensive gene expression data from various organs were generated and TPI biosynthesis related genes were extracted by principal component analysis (PCA). The metabolic pathway was assessed by comparing the coexpression network of TPI genes with the isoprenoid gene coexpression network of model plants. By PCA, we dissected 27 genes assumed to be involved in polyisoprene biosynthesis, including *TIDS* genes, genes encoding enzymes of the mevalonate (MVA) pathway and the 2-*C*-methyl-D-erythritol 4-phosphate (MEP) pathway, and genes related to rubber synthesis. The coexpression network revealed that 22 of the 27 TPI biosynthesis genes are coordinately expressed. The network was clustered into two modules, and this was also observed in model plants. The first module was mainly comprised of MEP pathway genes and *TIDS1* gene, and the second module, of MVA pathway genes and *TIDS5* gene. These results indicate that TPI is likely biosynthesized by both the MEP and MVA pathways and that *TIDS* gene expression is differentially controlled by these pathways.

Key words: coexpression network, *Eucommia ulmoides*, principal component analysis, *trans*-1,4-polyisoprene.

Eucommia ulmoides Oliver (Eucommiaceae) is a species producing *trans*-1,4-polyisoprene (TPI) throughout its tissues. Because this plant species has been artificially planted widely in East Asia (China, Korea, and Japan) and has ideal characteristics for efficient production of TPI, such as fast growth, high TPI content, and high molecular weight of TPI, it has been proposed as a candidate source for commercial TPI production (Nakazawa et al. 2009). TPI is a non-petroleum-based material that possesses more elasticity with resistance to biological degradation than *cis*-polyisoprene (natural rubber), and based on these characteristics, TPI has been used for cables, golf balls and other materials (Nakazawa et al. 2009; Tangpakdee et al. 1997; Tsujimoto et al. 2014).

TPI is an isoprenoid metabolite thought to be synthesized using isopentenyl diphosphate (IPP) as substrate (Bamba et al. 2010). IPP is synthesized by two pathways: the mevalonate (MVA) pathway in the cytoplasm (mitochondria and endoplasmic reticulum) and the 2-*C*-methyl-D-erythritol 4-phosphate (MEP) pathway in the chloroplast (Vranová et al. 2012). Based on analysis of expressed sequence tags (ESTs) of *E. ulmoides*, both isoprenoid synthesizing gene candidates and putative *trans*-isoprenyl diphosphate synthase (*TIDS*) genes were identified (Suzuki et al. 2012). Among the *TIDS*s, *TIDS2* and *4* were confirmed as having farnesyl diphosphate synthase (*FDPS*) activity (Kajiura et al. 2017; Suzuki et al. 2012). Other putative genes, *TIDS1*, *3*, and *5*, which have sequences similar to *FDPS*, do not complement *FDPS* genes; these genes might be

Abbreviations: ABA, abscisic acid; ACAT, Acetyl-CoA C-acetyltransferase; DMAPP, dimethylallyl diphosphate; DXPS, 1-deoxy-D-xylulose 5-phosphate synthase; FDPS, farnesyl diphosphate synthase; GAPDH, glyceraldehyde 3-phosphate dehydrogenase; GPPS, geranylgeranyl diphosphate synthase; GGPPS, geranylgeranyl pyrophosphate synthase; HDR, 4-hydroxy-3-methyl-2-butenyl-diphosphate reductase; HMGCR, 3-hydroxyl-3-mehylglutaryl-CoA reductase; HMGCS, 3-hydroxy-3-methylglutaryl-CoA synthase; IAA, indole-3-acetic acid; IDI, isopentenyl diphosphate isomerase; MEP, the 2-*C*-methyl-D-erythritol 4-phosphate; MVK, mevalonate kinase; MLP, major latex protein; MVA, mevalonate; MVD, Diphosphomevalonate decarboxylase; NPA, naphthylphthalamic acid; PCA, principal component analysis; REF, rubber elongation factor; SRPP, small rubber particle protein; TIDS, *trans*-isoprenyl diphosphate synthase; TPI, *trans*-1,4-polyisopren.

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This article can be found at http://www.jspcmb.jp/
Published online September 27, 2017

long-chain *trans*-polyprenyl diphosphate synthases in *E. ulmoides* (Suzuki et al. 2012). However, these genes have not been characterized and the mechanism of TPI biosynthesis through the MVA and MEP pathways is unclear.

In contrast to model plants, progress in identifying the functions of genes in trees is slow because of the limited research approaches and the small number of researchers. Under such circumstances, microarray analysis has been used to analyze the global gene expression pattern in various plant organs, and functionally similar genes and organ-specific genes have been grouped by multivariate analysis, such as principal component analysis (PCA) (Chow et al. 2007; Fasoli et al. 2012). Based on PCA, unique functional genes in specific organs have been identified (Fasoli et al. 2012). Furthermore, because genes in the same metabolic pathway are often coexpressed, genes of unknown function are sometimes identified as putatively related to the pathway based on coexpression network modeling (Hirai et al. 2007; Wille et al. 2004). As several studies of *Arabidopsis thaliana* have revealed a specific coexpression pattern in both the MVA and MEP pathways (Wille et al. 2004), using multivariate analysis and comparing the isoprenoid coexpression network of model plants to the non-model plant *E. ulmoides* might reveal the functions of uncharacterized genes including *TIDS1*, *3*, and *5* and address a major aspect of TPI biosynthesis.

Our goals of this study were (1) to classify the gene expression pattern into several functional gene groups by PCA by searching for putative *trans*-1,4-polyisoprene biosynthesis related genes in transcriptional data of various samples, and (2) to assess the gene coexpression network of the two isoprenoid pathways of *E. ulmoides* by comparing it to the isoprenoid related gene networks in two model plants: *A. thaliana* and *Oryza sativa*.

To obtain expression data, 102 samples from two individual *E. ulmoides* plants including both male and female were obtained in 2008 and 2009. The individuals were planted in soil at an elevation 1.65 m above sea level at a Hitachi Zosen Corporation factory (34°37′56″N, 135°27′27″E) in Osaka, Japan. The tree heights were approximately 10 m. Among the samples, 56 were comprised of six types of tissue: six inner stem tissues, six outer stem tissues, 20 female reproductive organs (flower or immature fruit) sampled during different seasons, three male flowers, 12 male leaves, and nine female leaves. The other 46 samples were comprised of tissues following various hormone, temperature, and light treatments: 25 fruit were given one of five treatments including three hormones (indole-3-acetic acid (IAA), naphthylphthalamic acid (NPA), combination of IAA and NPA, abscisic acid (ABA), and no-hormone control) for five treatment times (0, 3, 6, 12, and 24 h); 15 leaves were treated by combinations of two temperatures (27 and 37°C) and two lighting conditions (light and dark); six leaves were treated at one of two temperatures (15 and 42°C) under field lighting conditions. For a detailed description of samples, refer to Supplementary Table 1.

For dissecting gene expression characteristics, total RNA was prepared from each frozen sample. Each sample was ground into powder using a mortar and pestle, and RNA was extracted from about 200 mg using an RNeasy Plant Mini Kit (Qiagen, Hilden, Germany). The extracted RNA was treated with DNase I using an RNase-Free DNase Set (Qiagen), and RNA quantity and quality were checked by a NanoDrop 1000 spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA) and an Agilent Bioanalyzer 2100 electrophoresis system (Agilent Technologies, Inc., Santa Clara, CA, USA), respectively.

The DNA microarray was designed using the eArray program (Agilent Technologies) using EST information for this species (accessions FY896671-FY925126). The custom array (4×44 K platform) contains 10456 60-mer probes, and the probe sequences on the microarray were automatically designed by the algorithms of the eArray program based on 10,456 non-redundant tentative transcribed sequences (contigs and singlets) of this species (Suzuki et al. 2012). RNA was labeled by Cy3 dye using a Low RNA Input Linear Amplification Kit (Agilent Technologies) and the resultant cRNA probe quality was analyzed using an RNA 6000 Nano Assay Kit, and hybridization and washing were conducted using Gene Expression hybridization kit and wash buffer kit, respectively (Agilent Technologies). Hybridized slides were scanned using an Agilent G2505B scanner at a resolution of 5 μM at a wavelength of 532 nm, corresponding to the Cy3 emission wavelength. The microarray images were imported into Agilent Feature Extraction software v.9.5.3, and the signal intensity of each probe was obtained. The data discussed in this publication have been deposited in NCBI's Gene Expression Omnibus (Edgar et al. 2002) and are accessible through GEO Series accession number GSE97899. The obtained data were normalized using median and first and third quantiles for further analysis.

To separate the 10,456 genes of the 102 samples into similar expression groups, principal component analysis (PCA) was conducted by R ver. 3.2.0 software (R Core Team 2015). Annotations of the contributing genes for the first to third principal components (PCs) were assigned by the BLASTX program against proteins with an E-value of $1.0E^{-10}$ or better.

The first PC (PC1) represents 75.2% (standard deviation, 8.80) of the variability and this score was higher by far than the other PCs: the second and third PCs (PC2 and PC3) explained 5.7% (standard deviation, 2.40) and 3.7% (standard deviation, 1.97) of

Table 1. Top 10 unigenes, showing scores for three principal component and putative function assigned from BLASTX search results.

Rank in each PC	Scores on each PC	Unigene	Putative function of unigene	Accession number	E-value*
PC1					
1	220.7	RB013_E23	Hypothetical protein	BAD46202	4.0.E-29
2	164.4	RB013_C03	Probable cytochrome P450 monooxygenase	T02955	3.0.E-60
3	141.2	Contig347	RNA-binding gricine-rich protein-1 (RGP-1c)	BAA03743	2.0.E-65
4	140.1	Contig2324	Polyubiquitin UBQ10	AAM98141	0.0.E+00
5	138.7	RB011_P05	Hypothetical protein PY01929	EAA21331	2.0.E-14
6	125.5	Contig529	Surface protein SdrI	AAM90673	1.0.E-22
7	122.8	Contig1709	Hypothetical protein AN5245.2	XP_662849	2.0.E-04
8	122.0	Contig1928	Glutamine synthetase	AAB61597	0.0.E+00
9	116.5	Contig343	PM28B protein	CAB56217	1.0.E-152
10	114.2	Contig1209	Light harvesting chlorophyll a/b-binding protein	BAA25396	1.0.E-102
PC2					
1	72.7	Contig529	Surface protein SdrI	AAM90673	1.0.E-22
2	41.3	Contig2875	Allergenic isoflavone reductase-like protein Bet v 6.0102	AAG22740	1.0.E-143
3	35.1	Contig105	Putative transcription factor	AAK69513	7.0.E-49
4	32.6	Contig343	PM28B protein	CAB56217	1.0.E-152
5	28.9	Contig505	Auxin-repressed protein-like protein ARP1	AAX84677	7.0.E-40
6	28.7	Contig3064	Auxin-repressed protein-like protein ARP1	AAX84677	7.0.E-30
7	28.6	Contig1628_1	Metallothionein-1 like protein	AAB70560	8.0.E-32
8	28.6	Contig117	DRM1 (Dormancy-associated protein 1)	NP_849720	1.0.E-30
9	28.6	Contig1726	Auxin-repressed protein-like protein ARP1	AAX84677	7.0.E-45
10	26.7	RT022_C16	Transposon protein, putative, CACTA, En/Spm sub-class	ABA99001	6.5.E-02
PC3					
1	35.8	RB032_I18	Metallothionein-like protein	CAA69624	7.0.E-21
2	30.9	Contig1454	Metallothionein-like protein	CAA69624	1.0.E-23
3	27.1	Contig1928	Glutamine synthetase	AAB61597	0.0.E+00
4	24.4	Contig1912	Major allergen Pru ar 1	O50001	4.0.E-49
5	24.2	Contig655	Inositol-3-phosphate synthase (Myo-inositol-1-phosphate synthase)	Q9LW96	0.0.E+00
6	23.6	RB013_H06	Hypothetical protein TTHERM_00411540	EAS00603	2.3.E+00
7	23.4	Contig459	RD22-like protein	AAV36561	1.0.E-120
8	21.2	Contig1474	Lipid transfer protein	AAQ96338	1.0.E-38
9	19.9	Contig2834	Cinnamic acid 4-hydroxylase	BAB71716	0.0.E+00
10	19.6	Contig2875	Allergenic isoflavone reductase-like protein Bet v 6.0102	AAG22740	1.0.E-143

* E-values of the best hit in BLASTX are shown.

the variability, respectively. Genes related to constitutive functions, such as cytochrome, ubiquitin, glutamine synthetase, photosynthesis (chlorophyll A–B binding protein gene), were over-represented in the list of genes contributing to the PC1 (Table 1). Hormone induced genes and stress response genes were represented in the list of genes contributing to the PC2 and other genes, such as lignin biosynthesis pathway genes and dehydration-related genes (i.e. dehydrin, a dehydration-responsive protein), had a high rank for PC2 (data not shown) (Table 1). Genes involved in secondary metabolism were represented in the list of genes contributing to the PC3 (Table 1). The rank of the most of polyisoprene synthesis genes in PC3 was higher than in other PCs. All *TIDS* genes positively contributed to PC3, however, some of these genes contributed negatively to the other PCs (Supplementary Table 2). Thus, the polyisoprene synthesis genes might contribute more to PC3 than to the other PCs.

Because the first three PCs explain 84.6% of the gene expression variability, global gene expression of the samples was plotted using the three PCs: fruit, hormone-treated fruit and stressed leaves showed convergence, while stem samples of both outer and inner tissues, female leaves, ovules and stamens were distributed widely (Figure 1). PC1 had a much larger variance (75.2%) than other PCs; this indicated that most of this data could be explained by PC1. We used the six types of tissue with different seasons for this analysis (Supplementary Table 1). Female reproductive organ and leaves had some convergence on higher scores of PC1 axis, however, inner and outer stem tissues, male flower and some female leaf distributed widely on lower scores (Figure 1). It might be suggested that the our analyzed samples with different tissues and sampling season resulted in the large differences of gene expression related to constitutive function, and the gene expression characteristics of each tissue resulted in large variances of PC1. On the other hand, PC2 represents hormone related genes and lignin synthesis genes, and hormone-treated reproductive organs and both outer and inner stem tissues had positive scores for PC2. For PC3, hormone-

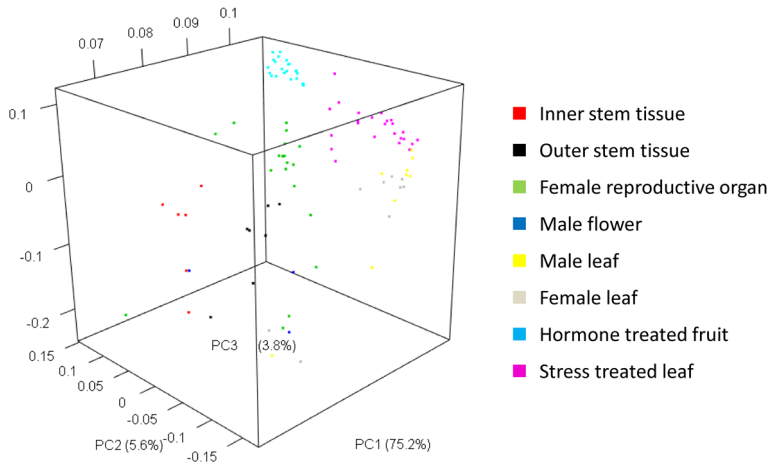

Figure 1. Score plot for PCA. Each colored point represents an individual tissue sample.

Table 2. List of genes obtained from coexpression network analysis, showing scores for third principal component (PC3).

Rank in PC3	Scores on PC3	Unigene ID	Putative product	Gene name	Module
45	9.28	RT019_M04	4-Hydroxy-3-methyl-2-butenyl diphosphate reductase	HDR*	1
50	8.57	Contig861	Isopentenyl diphosphate isomerase	IDI	1
52	8.55	Contig4112	Rubber elongation factor 2	REF2	1
93	5.81	Contig988	*trans*-Isoprenyl diphosphate synthase	TIDS1	1
104	5.47	Contig1438	*trans*-Isoprenyl diphosphate synthase	TIDS5	2
172	3.87	RE047_D18	Acetyl-CoA acetyltransferase 1	ACAT1	2
193	3.35	Contig1491	3-Hydroxy-3-methylglutaryl CoA synthase 1	HMGCS1	1
197	3.30	Contig1073	Rubber elongation factor 1	REF1	2
281	2.40	Contig3771	3-Hydroxy-3-methylglutaryl CoA synthase 2	HMGCS2	2
305	2.22	RT020_C19	Geranylgeranyl pyrophosphate synthase 2	GGPPS2	1
314	2.16	RT050_P19	Acetyl-CoA acetyltransferase 2	ACAT2	2
561	1.02	RB058_N12	1-Deoxy-D-xylulose 5-phosphate synthase 3	DXPS3	2
573	0.98	RT032_A10	3-Hydroxy-3-methylglutaryl CoA reductase 2	HMGCR2	2
1018	0.44	Contig3459	Diphosphomevalonate decarboxylase	MVD	2
1095	0.38	RT016_K07	Geranylgeranyl pyrophosphate synthase 1	GGPPS1	—
1115	0.38	Contig298	Mevalonate kinase	MVK	2
1281	0.30	RT023_E11	Farnesyl diphosphate synthase	TIDS4	2
1532	0.21	Contig3911	Farnesyl diphosphate synthase	TIDS2	—
1632	0.19	Contig2465	3-Hydroxy-3-methylglutaryl CoA reductase 1	HMGCR1	—
1862	0.14	RB033_C15	*trans*-Isoprenyl diphosphate synthase	TIDS3	—
2125	0.10	Contig3476	1-Deoxy-D-xylulose 5-phosphate synthase 1	DXPS1	—
2161	0.09	Contig2314	Geranylgeranyl diphospahte synthase	GPPS	—
2710	0.04	RB015F22	1-Deoxy-D-xylulose 5-phosphate synthase 2	DXPS2	2
2956	0.03	RT016_L11	1-Deoxy-D-xylulose 5-phosphate synthase 4	DXPS4	—
2973	0.03	Contig274	Major latex protein	MLP	—
3128	0.02	RT046_E14	Major latex protein-like	MLP-like*	—
3292	0.02	Contig4051	Rubber elongation factor-family protein	REF3*	—

* Newly identified genes in this study.

treated fruit and female reproductive organs had positive scores. In a previous study, each plant tissue also showed convergence in the PCA plot and each PC represented organ-specific gene expression (Fasoli et al. 2012). In *E. ulmoides*, accumulation of TPI is particularly observed in fruit (Nakazawa et al. 2009), so PC3 might reflect fruit-specific genes including those related to TPI biosynthesis.

The global gene expression pattern provides fundamental insight into how specific genes are involved in a biological event (Fasoli et al. 2012; Kang et al. 2011), and gene grouping is also useful for isolating genes involved in the same biological process such as a metabolic pathway (Basso et al. 2005; Hamada et al. 2011; Srinivasasainagendra et al. 2008). The multivariate analysis approach of PCA classifies multivariate gene expression data into mutually uncorrelated axes, and each of them has a different aspects of the samples (Ringnér 2008); thus, this method has been utilized for the grouping of the genes at the first step of classification of gene expression data without much computational

cost (Ma and Dai 2011; Ringnér 2008). However, another study has shown that gene grouping is not conducted well for PCs that account for many variations in the data (Yeung and Ruzzo 2001). In this study, PCA was conducted to extract gene groups from over 10,000 genes into three PCs, and PC3 had a much smaller variance (3.8%) than PC1 (75.2%), and successfully identified secondary metabolism genes including TPI biosynthesis related genes.

To detect the gene coexpression network of isoprenoid biosynthesis related genes, genes within PC3 were used for further network analysis. Referring to BLAST results, 27 genes related to isoprenoid biosynthesis were extracted from the genes within PC3; they included seven MVA pathway genes (acetyl-CoA C-acetyltransferase (*ACAT*), 3-methylglutaryl-CoA synthase (*HMGCS*), 3-hydroxyl-3-methylglutaryl-CoA reductase (*HMGCR*), mevalonate kinase (*MVK*), and mevalonate diphosphate (*MVD*)), one MEP pathway gene, 1-deoxy-D-xylulose 5-phosphate synthase (*DXPS*), the genes involved in branches of both pathways (isopentenyl pyrophosphate isomerase (*IDI*), geranylgeranyl diphosphate synthase (*GPPS*), *FDPS* and geranylgeranyl polyphosphate synthase (*GGPPS*)), and three natural rubber biosynthesis related genes (small rubber particle protein (*SRPP*), rubber elongation factor (*REF*), and major latex protein (*MLP*)); these genes have already been identified as isoprenoid biosynthetic genes by Suzuki et al. (2012). Three other polyisoprene synthesis genes were identified in this study: one from the MEP pathway, 4-hydroxy-3-methyl-2-butenyl diphosphate reductase (*HDR*) (Unigene: RT019_M04.b, Accession No: ABB55395, E-value: $3.0E^{-43}$), another encoding major latex-like protein (*MLP*-like) (Unigene: RT046_E14.b, Accession No: CAC83581, E-value: $8.0E^{-39}$), and the other encoding rubber elongation factor-family protein (*REF3*) (Unigene: Contig4051, Accession No: PF05755, E-value: $2.0E^{-32}$) (Table 2). Using these 27 genes, Pearson correlation coefficients (PCC) among all pairs of genes were calculated (Table 2). To search the specific coexpression network among isoprenoid biosynthesis related genes of *E. ulmoides*, the network structure was confirmed in 0.05 increments between PCC values of 0.50 (weak connection) and 0.70 (strong connection).

To compare the coexpression network for *E. ulmoides* polyisoprenoid biosynthesis to that of model plant species, we examined the gene coexpression network among isoprenoid synthesis genes of *A. thaliana* and *O. sativa*. Data were downloaded from the Gene Expression Omnibus for fitting to samples of *E. ulmoides* (Edgar et al. 2002). The data obtained from *A. thaliana* covered samples of 54 stems or shoots, 22 reproductive organs, 24 leaves, and 38 seedlings at different developmental stages or treated with heat or hormones; in total, there were 138 samples (Supplementary Table 3). Data from *O. sativa* covered samples of 14 stems or shoots, 45 reproductive organs, 43 leaves, and 10 seedlings at different developmental stages or treated with hormones; in total, there were 112 samples (Supplementary Table 4). From the data, 31 *A. thaliana* genes and 17 *O. sativa* genes related to isoprenoid biosynthesis were extracted (Supplementary Table 5) and the PCC was calculated among all pairs of these genes; the network structures were confirmed in 0.05 increments between PCC values of 0.50 and 0.70.

In *E. ulmoides*, 78% (21 of 27 genes) of the genes formed two coexpression network modules at a threshold PCC value of 0.65. The first module was comprised of *HDR*, *IDI*, *TIDS1*, *REF2*, *HMGCS1*, and *GGPPS2* genes and the second was comprised of *ACAT*, *HMGCS2*, *HMGCR2*, *MVK*, *MVD*, *DXPS*, *REF1*, *TIDS4*, and *TIDS5* genes (Figure 2). In *A. thaliana*, two network modules were also formed independently. The first module was comprised of seven genes of the MEP pathway (*DXPS*, *DXR*, *ISPD*, *CDPMEK*, *ISPF*, *HDS*, and *HDR*) and *GGPPS8*. The second module was mainly comprised of six genes of the MVA pathway (*ACAT3*, *HMGCS*, *HMGCR*, *MVK*, and *MVD1* and *2*), *IDI*, and *FDPS2* (Supplementary Figure 1). *O. sativa* also formed two independent network modules. The first module was comprised of five genes of the MEP pathway (*DXR*,

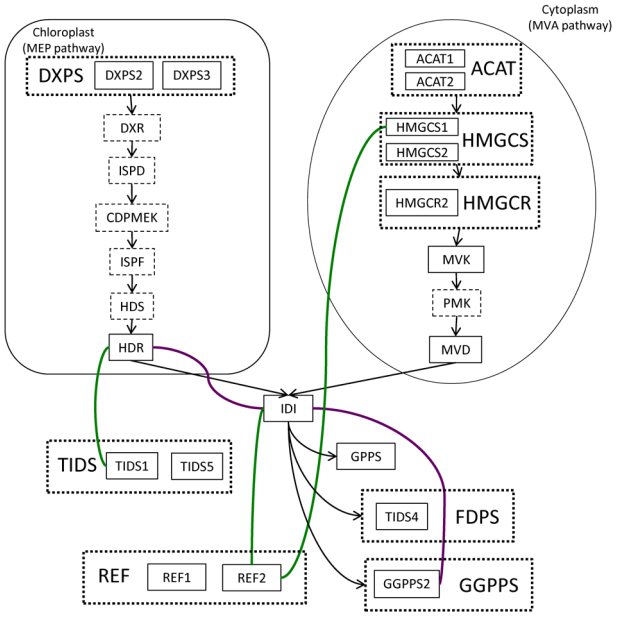

Figure 2. Coexpression network of the first modules found for isoprenoid pathway genes and potential rubber genes with the threshold PCC value of 0.65 or higher. Identified and unidentified unigenes are enclosed by solid and dotted lines, respectively. Metabolic flow is shown by arrows and coexpressed genes are connected by colored solid lines; green represents different and purple the same connections found in the networks of model plants. Genes with no connections to any genes have been omitted from the figure. For details of the genes used for network analysis, see Table 2.

ISPD, *CDPMEK*, *HDS*, and *HDR*) and *GPPS*. Four genes in the MVA pathway (*ACAT*, *HMGCS*, *HMGCR*, and *MVK*) and *FDPS2* constructed the second module (Supplementary Figure 2). In *E. ulmoides*, two modules were connected at a PCC value of 0.60; however, the modules of model plants did not connect at PCC scores from 0.50 to 0.70 (data not shown) suggesting that the connections of two modules of model plant species were weaker than that of *E. ulmoides*.

The network structure of all three species was divided into two modules. The first and second modules of the two model plants corresponded with the gene groups of the MEP and MVA pathway, respectively (Supplementary Figures 1 and 2). However, a few MEP pathway genes were identified in *E. ulmoides* and the structure of the first module of *E. ulmoides* did not correspond well to the MEP pathway genes. On the other hand, *GPPS* or *GGPPS* constituted the first module of all three plant species, and previous research also shows the coexpression network of isoprenoid pathway genes of *A. thaliana* divided into two modules corresponding to the MEP and MVA pathways (Wille et al. 2004). The coexpression network of isoprenoid biosynthesis tends to be divided into modules of MEP and MVA pathway genes, and thus, the first module of *E. ulmoides* may also represent the MEP pathway gene groups.

Connections were observed between the MEP and MVA pathway genes of *E. ulmoides*: *HMGCS1* is coexpressed with an MEP pathway gene via *REF2* in the first module, and *DXPS* is coexpressed with *ACAT* (Figure 3). Although genes from the two pathways are distributed in different organelles (MEP pathway genes in the chloroplast; MVA pathway genes in the cytosolic, endoplasmic reticulum and peroxisome compartments (Vranová et al. 2012)), cross-talk via IPP is confirmed in several species (Hemmerlin et al. 2003; Laule et al. 2003) and the previous study of the coexpression network in *A. thaliana* also found a connection between genes in the MEP and MVA pathways: between the gene for *DXPS* and one of the MVA pathway genes, *MVD*, and between genes encoding *IDI* and *HDS* of the MEP pathway (Wille et al. 2004). *E. ulmoides* also shares IPP between the MEP and MVA pathways, indicating connections between these pathways (Bamba et al. 2010); the results of our network analysis supported these connections between the MEP and MVA pathways in *E. ulmoides*. Furthermore, these connections were not observed in the model plants of our study. In contrast to *E. ulmoides*, these model plants do not biosynthesize TPI or other polyisoprenes, indicating that the interaction between the MEP and MVA pathways or the cross-talk of IPP may be more active in *E. ulmoides* than in these model plants.

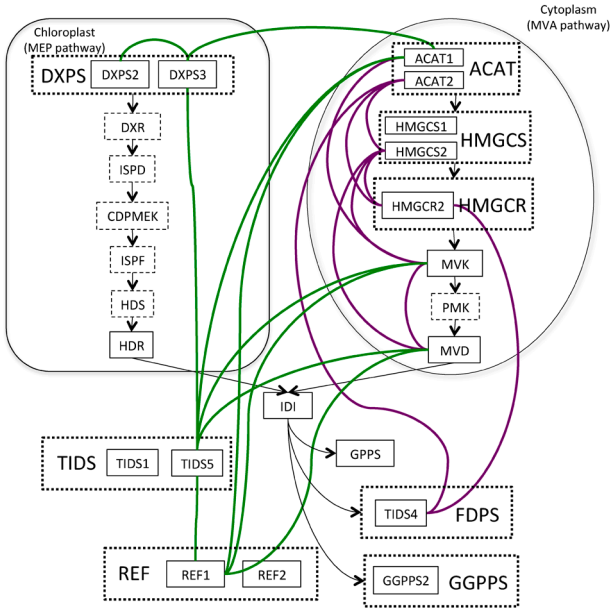

Figure 3. Coexpression network of the second module of isoprenoid pathway genes and potential rubber genes above the threshold PCC value of 0.65. For explanations of the lines and gene names, see the legends of Figure 2 and Table 2, respectively.

Different *REF* and *TIDS* genes constituted each module: the first module has *REF2* and *TIDS1*; the second module, *REF1* and *TIDS5* (Figures 2 and 3). The functions of TIDSs are still unknown; however, rubber formation related genes, *REF*s, contribute to forming *cis*-polyisoprene in over one micrometer aggregates (Berthelot et al. 2014). Some products downstream of the MEP and MVA pathways in model plants differ (MEP pathway, monoterpenoids, carotenoids; MVA pathway, squalene (Dubey et al. 2003; Vranová et al. 2012; Wille et al. 2004)); however, several products such as sesquiterpenes and polyprenols are synthesized via both pathways (Vranová et al. 2012). A previous study found that ^{13}C labeled TPI of *E. ulmoides* is obtained from both pathways, indicating that TPI biosynthesis is conducted through two pathways (Bamba et al. 2010). The module connections between each gene in the pathways and the set of each *TIDS* and *REF* gene indicate that a combination of *TIDS1* and *REF2* is presumably involved in TPI production using IPP mainly from the MEP pathway, and a combination of *TIDS5* and *REF1* using IPP mainly from the MVA pathway. On the other hand, it was not suggested which is the primary pathway of TPI biosynthesis. Previous EST analysis shows that the High *TIDS1* expression is observed in mature leaves and stems and *TIDS5* expression is observed in young leaves and stems (Suzuki et al. 2012). These results suggest that the primary pathway of TPI biosynthesis could be changed among the tissues with different growing stages.

Coexpression network analysis has demonstrated the power to identify genes involved in the same biological process (Hirai et al. 2007; Liu et al. 2009; Sasaki-Sekimoto et al. 2005; van Waveren and Moraes 2008; Walhout et al. 2002). Since genes involved in the same

biological process are often co-regulated in a similar spatiotemporal manner, coexpression analysis can identify critical genetic information associated with the process. In particular, genes involved in secondary metabolite pathways are more likely to be detected than in primary metabolite pathways because primary metabolites constitutively active, whereas secondary metabolism tends to be activated under particular circumstances (Hirai et al. 2007). Hirai et al. (2007) suggest that secondary metabolites are controlled by a small number of regulatory elements, and this might allow the detection of genes related to secondary metabolites. Indeed, TPI is likely to be accumulated in plant tissue when fertilizers with Mg^{2+} and Ca^{2+} are supplied, and these divalent cations and thiamine pyrophosphate are essential for activation of genes in the MEP and MVA pathways (Dubey et al. 2003; Eisenreich et al. 2004). Thus, these factors affecting expression of genes in isoprene biosynthesis may allow identification of extraction of corresponding gene groups by PCA and detection of genes of unknown function such as the *TIDS*s and *REF*s involved in both the MEP and MVA pathways.

These results might confirm the suitability of PCA and subsequent coexpression network analysis based on PCC scores in non-model plants to estimate the function of unknown genes before the molecular characterization of each gene. However, only two genes in the MEP pathway of *E. ulmoides* have been identified: *DXPS*, in Suzuki et al. (2012), and *HDR*, in this study, so an overview of the MEP pathway gene coexpression network is still incomplete. Further studies of the coexpression of the entire genome, including the MEP pathway genes, and characterization of *TIDS*s and *REF*s might reveal the details of TPI biosynthesis.

Acknowledgements

This study was partly supported by New Energy and Industrial Technology Development Organization, Japan.

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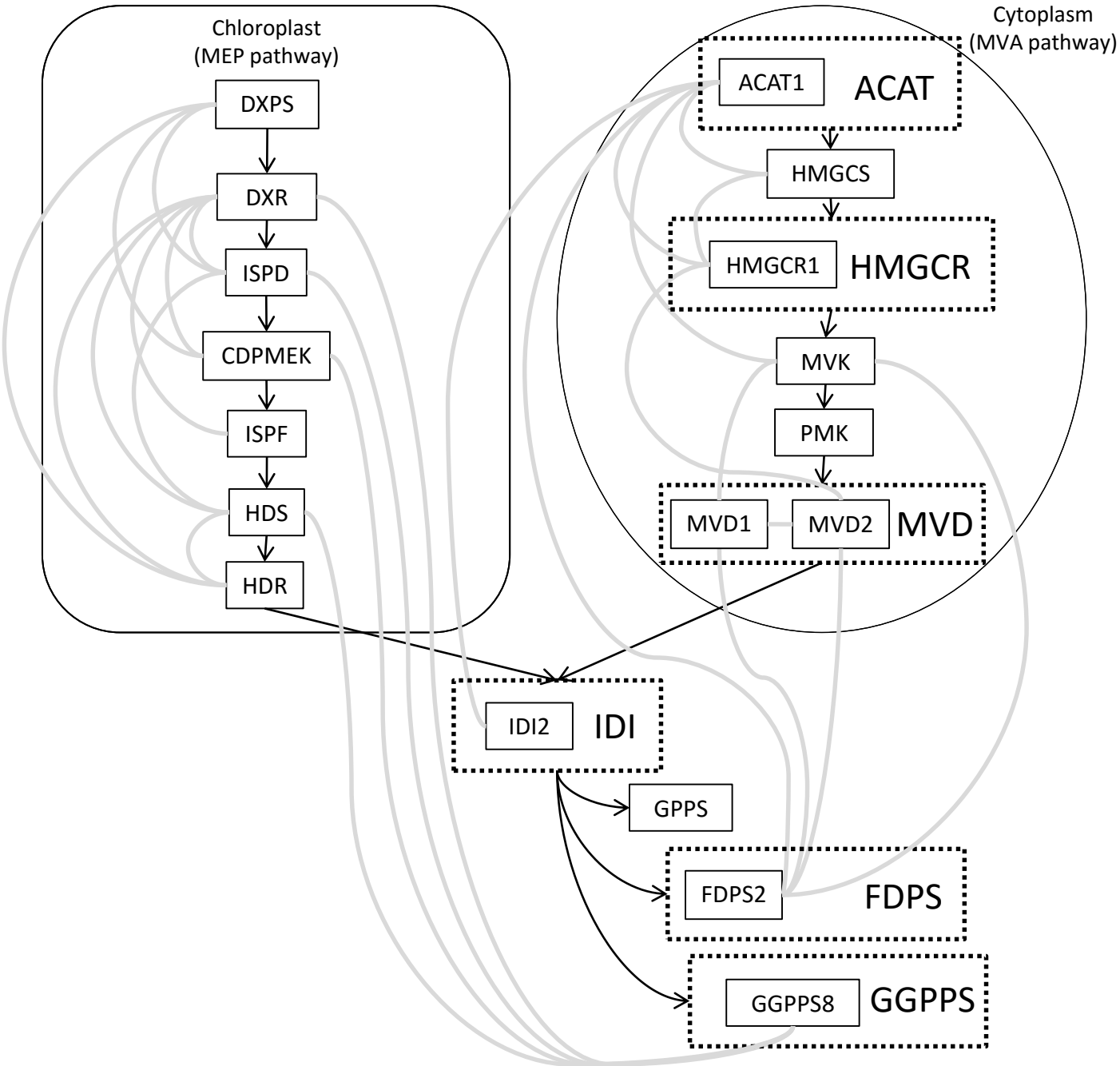
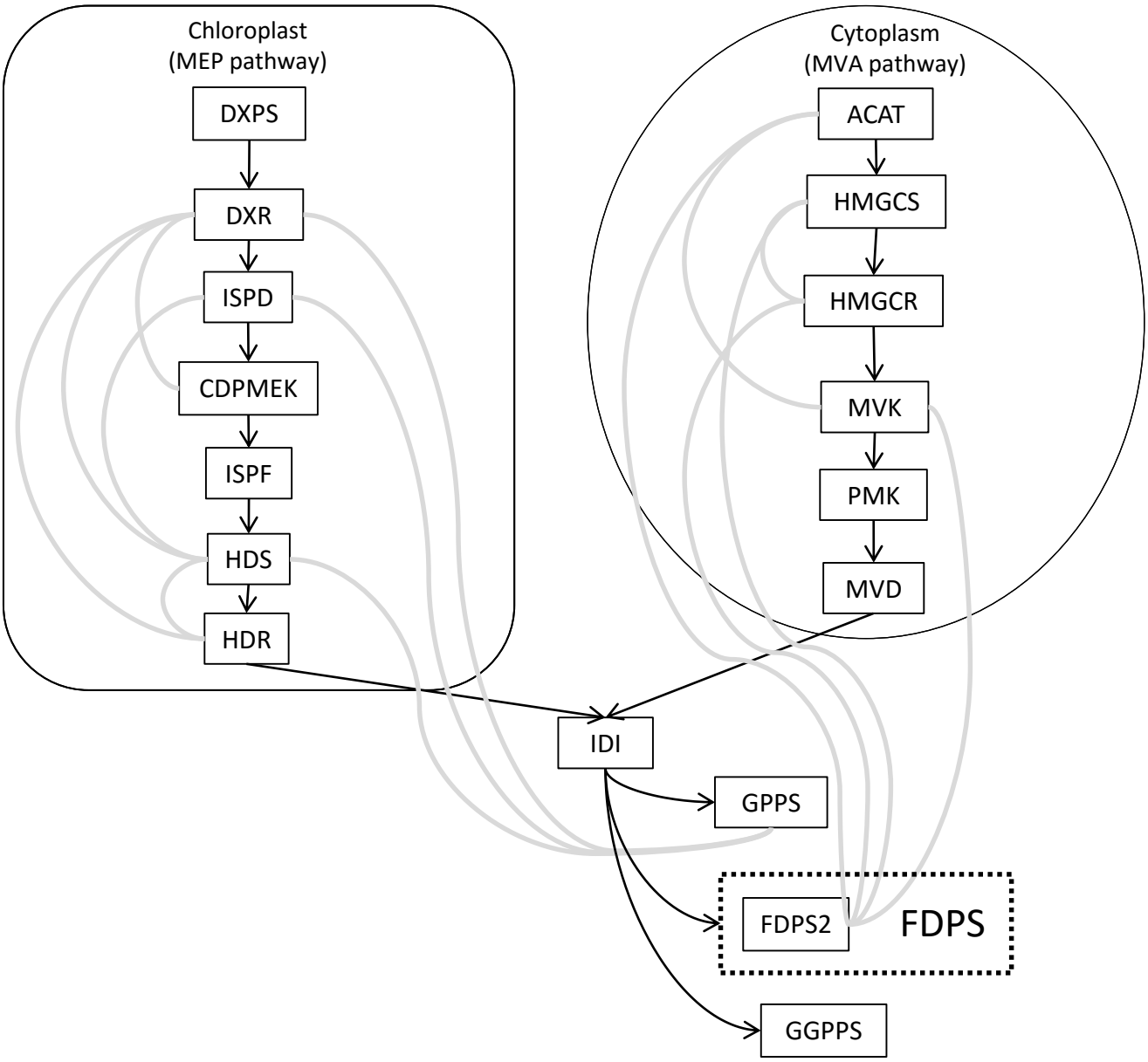


Supplementary Figure 1. Coexpression network of the isoprenoid pathway genes of *Arabidopsis thariana* with 0.65 PCC value. Solid lines represent the coexpression connections from the PCC analysis. The genes used for the network analysis were listed in Supplementary Table 4 and the genes which did not have any connection to other genes were omitted from figure.



Supplementary Figure 2. Coexpression network of the isoprenoid pathway genes of *Oryza sativa* with 0.65 PCC value. The genes used for the analysis were listed in Supplementary Table 4.

Supplementary Table 1. Sample tissue information for DNA microarray analysis

No.	Sample tissue	Sex	Sample description	Season	Sampling date
1	Inner stem tissue	Male	Inner stem tissue, current year	Mid-spring	22-Apr-08
2	Inner stem tissue	Male	Inner stem tissue, current year	Late-spring	27-May-08
3	Inner stem tissue	Male	Inner stem tissue, current year	Early-summer	24-Jun-08
4	Inner stem tissue	Male	Inner stem tissue, current year	Early-autumn	01-Oct-08
5	Inner stem tissue	Male	Inner stem tissue, current year	Mid-winter	13-Jan-08
6	Inner stem tissue	Male	Inner stem tissue, 2nd year	Mid-spring	23-Apr-08
7	Outer stem tissue	Male	Outer stem tissue, current year	Mid-spring	22-Apr-08
8	Outer stem tissue	Male	Outer stem tissue, current year	Late-spring	27-May-08
9	Outer stem tissue	Male	Outer stem tissue, current year	Early-summer	24-Jun-08
10	Outer stem tissue	Male	Outer stem tissue, current year	Early-autumn	01-Oct-08
11	Outer stem tissue	Male	Outer stem tissue, current year	Mid-winter	13-Jan-08
12	Outer stem tissue	Male	Outer stem tissue, 2nd year	Mid-spring	23-Apr-08
13	Female flower/fruit	Female	Immature fruit	Early-summer	10-Jun-08
14	Female flower/fruit	Female	Immature fruit	Early-summer	24-Jun-08
15	Female flower/fruit	Female	Immature fruit	Mid-summer	08-Jul-08
16	Female flower/fruit	Female	Immature fruit	Mid-summer	22-Jul-08
17	Female flower/fruit	Female	Immature fruit	Late-summer	05-Aug-08
18	Female flower/fruit	Female	Immature fruit	Late-summer	19-Aug-08
19	Female flower/fruit	Female	Immature fruit	Early-autumn	04-Sep-08
20	Female flower/fruit	Female	Immature fruit	Early-autumn	16-Sep-08
21	Female flower/fruit	Female	Immature fruit	Mid-autumn	01-Oct-08
22	Female flower/fruit	Female	Immature fruit	Mid-autumn	16-Oct-08
23	Female flower/fruit	Female	Immature fruit	Mid-autumn	28-Oct-08
24	Female flower/fruit	Female	Immature fruit	Mid-autumn	28-Oct-08
25	Female flower/fruit	Female	Wing of immature fruit	Early-summer	10-Jun-08
26	Female flower/fruit	Female	Immature fruit without wing	Early-summer	10-Jun-08
27	Female flower/fruit	Female	Female flower	Mid-spring	08-Apr-08
28	Female flower/fruit	Female	Female flower	Mid-spring	11-Apr-08
29	Female flower/fruit	Female	Female flower	Mid-spring	22-Apr-08
30	Female flower/fruit	Female	Female flower	Mid-spring	28-Apr-08
31	Female flower/fruit	Female	Female flower	Late-spring	13-May-08
32	Female flower/fruit	Female	Female flower	Late-spring	27-May-08
33	Male flower	Male	Male flower	Early-spring	24-Mar-08
34	Male flower	Male	Male flower	Mid-spring	01-Apr-08
35	Male flower	Male	Male flower	Mid-spring	11-Apr-08
36	Male leaf	Male	Leaf	Early-summer	19-Jun-08
37	Male leaf	Male	Leaf	Early-summer	19-Jun-08
38	Male leaf	Male	Leaf	Early-summer	19-Jun-08
39	Male leaf	Male	Leaf bud	Early-spring	24-Mar-08
40	Male leaf	Male	Leaf	Mid-spring	11-Apr-08
41	Male leaf	Male	Leaf	Mid-spring	28-Apr-08
42	Male leaf	Male	Leaf	Late-spring	27-May-08
43	Male leaf	Male	Leaf	Early-summer	24-Jun-08
44	Male leaf	Male	Leaf	Mid-summer	22-Jul-08
45	Male leaf	Male	Leaf	Late-summer	19-Aug-08
46	Male leaf	Male	Leaf	Early-autumn	16-Sep-08
47	Male leaf	Male	Leaf	Mid-autumn	28-Oct-08
48	Female leaf	Female	Leaf bud	Early-spring	24-Mar-09
49	Female leaf	Female	Leaf	Mid-spring	11-Apr-09
50	Female leaf	Female	Leaf	Mid-spring	28-Apr-08
51	Female leaf	Female	Leaf	Late-spring	27-May-08
52	Female leaf	Female	Leaf	Early-summer	24-Jun-08
53	Female leaf	Female	Leaf	Mid-summer	22-Jul-08
54	Female leaf	Female	Leaf	Late-summer	19-Aug-08
55	Female leaf	Female	Leaf	Early-autumn	16-Sep-08
56	Female leaf	Female	Leaf	Mid-autumn	28-Oct-08
57	Hormon treated fruit	Female	Fruit treated nothing for 0hr (control)	Late-spring	30-May-08
58	Hormon treated fruit	Female	Fruit treated nothing for 3hr (control)	Late-spring	30-May-08
59	Hormon treated fruit	Female	Fruit treated nothing for 6hr (control)	Late-spring	30-May-08
60	Hormon treated fruit	Female	Fruit treated nothing for 12hr (control)	Late-spring	30-May-08

Supplementary Table 1. Continued

61	Hormon treated fruit	Female	Fruit treated nothing for 24hr (control)	Late-spring	30-May-08
62	Hormon treated fruit	Female	Fruit treated 10μM IAA for 0hr	Late-spring	30-May-08
63	Hormon treated fruit	Female	Fruit treated 10μM IAA for 3hr	Late-spring	30-May-08
64	Hormon treated fruit	Female	Fruit treated 10μM IAA for 6hr	Late-spring	30-May-08
65	Hormon treated fruit	Female	Fruit treated 10μM IAA for 12hr	Late-spring	30-May-08
66	Hormon treated fruit	Female	Fruit treated 10μM IAA for 24hr	Late-spring	30-May-08
67	Hormon treated fruit	Female	Fruit treated 10μM IAA + 20mM NPA for 0hr	Late-spring	30-May-08
68	Hormon treated fruit	Female	Fruit treated 10μM IAA + 20mM NPA for 3hr	Late-spring	30-May-08
69	Hormon treated fruit	Female	Fruit treated 10μM IAA + 20mM NPA for 6hr	Late-spring	30-May-08
70	Hormon treated fruit	Female	Fruit treated 10μM IAA + 20mM NPA for 12hr	Late-spring	30-May-08
71	Hormon treated fruit	Female	Fruit treated 10μM IAA + 20mM NPA for 24hr	Late-spring	30-May-08
72	Hormon treated fruit	Female	Fruit treated 20μM NPA for 0hr	Late-spring	30-May-08
73	Hormon treated fruit	Female	Fruit treated 20μM NPA for 3hr	Late-spring	30-May-08
74	Hormon treated fruit	Female	Fruit treated 20μM NPA for 6hr	Late-spring	30-May-08
75	Hormon treated fruit	Female	Fruit treated 20μM NPA for 12hr	Late-spring	30-May-08
76	Hormon treated fruit	Female	Fruit treated 20μM NPA for 24hr	Late-spring	30-May-08
77	Hormon treated fruit	Female	Fruit treated 10μM ABA for 0hr	Late-spring	30-May-08
78	Hormon treated fruit	Female	Fruit treated 10μM ABA for 3hr	Late-spring	30-May-08
79	Hormon treated fruit	Female	Fruit treated 10μM ABA for 6hr	Late-spring	30-May-08
80	Hormon treated fruit	Female	Fruit treated 10μM ABA for 12hr	Late-spring	30-May-08
81	Hormon treated fruit	Female	Fruit treated 10μM ABA for 24hr	Late-spring	30-May-08
82	Stress treated leaf	Male	Leaf treated 37°C under bright field, 0hr	Early-summer	10-Jun-08
83	Stress treated leaf	Male	Leaf treated 37°C under bright field, 3hr	Early-summer	10-Jun-08
84	Stress treated leaf	Male	Leaf treated 37°C under bright field, 24hr	Early-summer	10-Jun-08
85	Stress treated leaf	Male	Leaf treated 37°C in the dark, 0hr	Early-summer	10-Jun-08
86	Stress treated leaf	Male	Leaf treated 37°C in the dark, 3hr	Early-summer	10-Jun-08
87	Stress treated leaf	Male	Leaf treated 37°C in the dark, 24hr	Early-summer	10-Jun-08
88	Stress treated leaf	Male	Leaf treated 27°C under bright field, 0hr	Early-summer	17-Jun-08
89	Stress treated leaf	Male	Leaf treated 27°C under bright field, 3hr	Early-summer	17-Jun-08
90	Stress treated leaf	Male	Leaf treated 27°C under bright field, 24hr	Early-summer	17-Jun-08
91	Stress treated leaf	Male	Leaf treated 27°C in the dark, 0hr	Early-summer	17-Jun-08
92	Stress treated leaf	Male	Leaf treated 27°C in the dark, 3hr	Early-summer	17-Jun-08
93	Stress treated leaf	Male	Leaf treated 27°C in the dark, 24hr	Early-summer	17-Jun-08
94	Stress treated leaf	Male	Leaf treated 27°C in the dark, 0hr	Early-summer	19-Jun-08
95	Stress treated leaf	Male	Leaf treated 27°C in the dark, 3hr	Early-summer	19-Jun-08
96	Stress treated leaf	Male	Leaf treated 27°C in the dark, 24hr	Early-summer	19-Jun-08
97	Stress treated leaf	Male	Leaf treated 42°C under bright field, 0hr	Early-summer	24-Jun-08
98	Stress treated leaf	Male	Leaf treated 42°C under bright field, 3hr	Early-summer	24-Jun-08
99	Stress treated leaf	Male	Leaf treated 42°C under bright field, 24hr	Early-summer	24-Jun-08
100	Stress treated leaf	Male	Leaf treated 15°C under bright field, 0hr	Mid-summer	22-Jul-08
101	Stress treated leaf	Male	Leaf treated 15°C under bright field, 3hr	Mid-summer	22-Jul-08
102	Stress treated leaf	Male	Leaf treated 15°C under bright field, 24hr	Mid-summer	22-Jul-08

Supplementary Table 2. Rank and scores for each principal component (PC) of polyisoprene synthesis gene

Gene name	Rank in PC3	Scores on PC3	Rank in PC1	Scores on PC1	Rank in PC2	Scores on PC2
HDR	45	9.28	213	22.88	10333	-5.75
IDI	50	8.57	262	19.71	10283	-4.07
REF2	52	8.55	186	26.51	10304	-4.51
TIDS1	93	5.81	223	22.49	10397	-12.47
TIDS5	104	5.47	763	6.58	63	7.73
ACAT1	172	3.87	410	13.33	106	5.12
HMGCS1	193	3.35	349	15.45	9924	-1.11
REF1	197	3.30	309	17.25	164	3.64
HMGCS2	281	2.40	1221	2.74	859	0.51
GGPPS2	305	2.22	1778	0.65	6690	0.02
ACAT2	314	2.16	777	6.35	9713	-0.71
DXPS3	561	1.02	1988	0.17	636	0.81
HMGCR2	573	0.98	2033	0.09	8716	-0.12
MVD	1018	0.44	1092	3.58	307	1.95
GGPPS1	1095	0.38	2231	-0.25	9373	-0.37
MVK	1115	0.38	1896	0.37	691	0.71
TIDS4	1281	0.30	3998	-1.97	8279	-0.05
TIDS2	1532	0.21	1207	2.84	9952	-1.18
HMGCR1	1632	0.19	3397	-1.61	1294	0.29
TIDS3	1862	0.14	2754	-1.02	8531	-0.09
DXPS1	2125	0.10	3486	-1.67	8521	-0.08
GPPS	2161	0.09	4606	-2.26	9155	-0.25
DXPS2	2710	0.04	6775	-2.74	3129	0.06
DXPS4	2956	0.03	8483	-2.89	3447	0.05
MLP	2973	0.03	9970	-2.93	4191	0.04
MLP-like	3128	0.02	1682	0.95	249	2.38
REF3	3292	0.02	5575	-2.54	6401	0.02

Supplementary Table 3. Samples used for network analysis of *Arabidopsis thaliana* .

No.	Platform ID	Series ID	Sample ID	Sample tissue	Sample description
1	GPL198	GSE2478	GSM61037	Stem/shoot	Stem base, first internode
2	GPL198	GSE2478	GSM61037	Stem/shoot	Stem base, first internode
3	GPL198	GSE2478	GSM61037	Stem/shoot	Stem base, first internode
4	GPL198	GSE2478	GSM61038	Stem/shoot	Stem base, first internode
5	GPL198	GSE2478	GSM61038	Stem/shoot	Stem base, first internode
6	GPL198	GSE2478	GSM61038	Stem/shoot	Stem base, first internode
7	GPL198	GSE2476	GSM60988	Stem/shoot	Stem
8	GPL198	GSE2476	GSM60988	Stem/shoot	Stem
9	GPL198	GSE2476	GSM60988	Stem/shoot	Stem
10	GPL198	GSE5633	GSM13164	Stem/shoot	Shoot and stem
11	GPL198	GSE5633	GSM13165	Stem/shoot	Shoot and stem
12	GPL198	GSE5633	GSM13165	Stem/shoot	Shoot and stem
13	GPL198	GSE5620	GSM13122	Stem/shoot	Shoot
14	GPL198	GSE5620	GSM13122	Stem/shoot	Shoot
15	GPL198	GSE5620	GSM13122	Stem/shoot	Shoot
16	GPL198	GSE5620	GSM13122	Stem/shoot	Shoot
17	GPL198	GSE5620	GSM13123	Stem/shoot	Shoot
18	GPL198	GSE5620	GSM13123	Stem/shoot	Shoot
19	GPL198	GSE5620	GSM13123	Stem/shoot	Shoot
20	GPL198	GSE5620	GSM13123	Stem/shoot	Shoot
21	GPL198	GSE5620	GSM13123	Stem/shoot	Shoot
22	GPL198	GSE5620	GSM13124	Stem/shoot	Shoot
23	GPL198	GSE5620	GSM13124	Stem/shoot	Shoot
24	GPL198	GSE5620	GSM13124	Stem/shoot	Shoot
25	GPL198	GSE5620	GSM13124	Stem/shoot	Shoot
26	GPL198	GSE5620	GSM13124	Stem/shoot	Shoot
27	GPL198	GSE5620	GSM13125	Stem/shoot	Shoot
28	GPL198	GSE5620	GSM13125	Stem/shoot	Shoot
29	GPL198	GSE5620	GSM13125	Stem/shoot	Shoot
30	GPL198	GSE5620	GSM13125	Stem/shoot	Shoot
31	GPL198	GSE1926	GSM47791	Stem/shoot	Shoot
32	GPL198	GSE1926	GSM47791	Stem/shoot	Shoot
33	GPL198	GSE5626	GSM13138	Stem/shoot	UV-B stress shoot
34	GPL198	GSE5626	GSM13138	Stem/shoot	UV-B stress shoot
35	GPL198	GSE5626	GSM13138	Stem/shoot	UV-B stress shoot
36	GPL198	GSE5626	GSM13138	Stem/shoot	UV-B stress shoot
37	GPL198	GSE5626	GSM13139	Stem/shoot	UV-B stress shoot
38	GPL198	GSE5626	GSM13139	Stem/shoot	UV-B stress shoot
39	GPL198	GSE5626	GSM13139	Stem/shoot	UV-B stress shoot
40	GPL198	GSE5626	GSM13139	Stem/shoot	UV-B stress shoot
41	GPL198	GSE5626	GSM13139	Stem/shoot	UV-B stress shoot
42	GPL198	GSE5626	GSM13140	Stem/shoot	UV-B stress shoot
43	GPL198	GSE5626	GSM13140	Stem/shoot	UV-B stress shoot
44	GPL198	GSE5626	GSM13140	Stem/shoot	UV-B stress shoot
45	GPL198	GSE5626	GSM13140	Stem/shoot	UV-B stress shoot
46	GPL198	GSE5626	GSM13140	Stem/shoot	UV-B stress shoot
47	GPL198	GSE5628	GSM13143	Stem/shoot	Heat stress shoot
48	GPL198	GSE5628	GSM13144	Stem/shoot	Heat stress shoot
49	GPL198	GSE5628	GSM13144	Stem/shoot	Heat stress shoot
50	GPL198	GSE5628	GSM13144	Stem/shoot	Heat stress shoot
51	GPL198	GSE5628	GSM13144	Stem/shoot	Heat stress shoot
52	GPL198	GSE5628	GSM13144	Stem/shoot	Heat stress shoot
53	GPL198	GSE5628	GSM13145	Stem/shoot	Heat stress shoot
54	GPL198	GSE5628	GSM13145	Stem/shoot	Heat stress shoot

Supplementary Table 3. Continued

55	GPL198	GSE2728	GSM67459	Reproductive organ	Unpollinated pistil
56	GPL198	GSE2728	GSM67459	Reproductive organ	Unpollinated pistil
57	GPL198	GSE2728	GSM67458	Reproductive organ	Pistil 0.5 hours after pollination
58	GPL198	GSE2728	GSM67458	Reproductive organ	Pistil 0.5 hours after pollination
59	GPL198	GSE2728	GSM67458	Reproductive organ	Pistil 3.5 hours after pollination
60	GPL198	GSE2728	GSM67459	Reproductive organ	Pistil 3.5 hours after pollination
61	GPL198	GSE2728	GSM67459	Reproductive organ	Pistil 8 hours after pollination
62	GPL198	GSE2728	GSM67459	Reproductive organ	Pistil 8 hours after pollination
63	GPL198	GSE2728	GSM67459	Reproductive organ	Ovule
64	GPL198	GSE2728	GSM67459	Reproductive organ	Ovule
65	GPL198	GSE5736	GSM13381	Reproductive organ	Silique
66	GPL198	GSE5736	GSM13381	Reproductive organ	Silique
67	GPL198	GSE5736	GSM13381	Reproductive organ	Silique
68	GPL198	GSE5736	GSM13381	Reproductive organ	Silique
69	GPL198	GSE5736	GSM13382	Reproductive organ	Silique
70	GPL198	GSE5736	GSM13382	Reproductive organ	Silique
71	GPL198	GSE5634	GSM13168	Reproductive organ	Silique and seed
72	GPL198	GSE5634	GSM13168	Reproductive organ	Silique and seed
73	GPL198	GSE5634	GSM13169	Reproductive organ	Silique and seed
74	GPL198	GSE4733	GSM10682	Reproductive organ	Stamen
75	GPL198	GSE4733	GSM10682	Reproductive organ	Stamen
76	GPL198	GSE4733	GSM10682	Reproductive organ	Stamen
77	GPL198	GSE5630	GSM13149	Leaf	Leaf
78	GPL198	GSE5630	GSM13149	Leaf	Leaf
79	GPL198	GSE5630	GSM13150	Leaf	Leaf
80	GPL198	GSE5630	GSM13150	Leaf	Leaf
81	GPL198	GSE5630	GSM13150	Leaf	Leaf
82	GPL198	GSE5630	GSM13151	Leaf	Leaf
83	GPL198	GSE5630	GSM13151	Leaf	Leaf
84	GPL198	GSE5630	GSM13151	Leaf	Leaf
85	GPL198	GSE5630	GSM13151	Leaf	Leaf
86	GPL198	GSE5630	GSM13152	Leaf	Leaf
87	GPL198	GSE5630	GSM13152	Leaf	Leaf
88	GPL198	GSE5630	GSM13152	Leaf	Leaf
89	GPL198	GSE5630	GSM13153	Leaf	Leaf
90	GPL198	GSE5630	GSM13153	Leaf	Leaf
91	GPL198	GSE5630	GSM13153	Leaf	Leaf
92	GPL198	GSE5630	GSM13154	Leaf	Leaf
93	GPL198	GSE5630	GSM13154	Leaf	Leaf
94	GPL198	GSE5630	GSM13154	Leaf	Leaf
95	GPL198	GSE5630	GSM13154	Leaf	Leaf
96	GPL198	GSE5630	GSM13155	Leaf	Leaf
97	GPL198	GSE5521	GSM12868	Leaf	Rosette leaf
98	GPL198	GSE5521	GSM12868	Leaf	Rosette leaf
99	GPL198	GSE5521	GSM12869	Leaf	Rosette leaf
100	GPL198	GSE5521	GSM12869	Leaf	Rosette leaf
101	GPL198	GSE3326	GSM74894	Seedling	Seedling treated at 0 °C for 0 hr (control)
102	GPL198	GSE3326	GSM74902	Seedling	Seedling treated at 0 °C for 0 hr (control)
103	GPL198	GSE3326	GSM74896	Seedling	Seedling treated at 0 °C for 3 hr
104	GPL198	GSE3326	GSM74904	Seedling	Seedling treated at 0 °C for 3 hr
105	GPL198	GSE3326	GSM74898	Seedling	Seedling treated at 0 °C for 6 hr
106	GPL198	GSE3326	GSM74906	Seedling	Seedling treated at 0 °C for 6 hr
107	GPL198	GSE3326	GSM74900	Seedling	Seedling treated at 0 °C for 24 hr
108	GPL198	GSE3326	GSM74908	Seedling	Seedling treated at 0 °C for 24 hr

Supplementary Table 3. Continued

109	GPL198	GSE3938	GSM96713	Seedling	Seedling treated with IAA for 30 min
110	GPL198	GSE3938	GSM96713	Seedling	Seedling treated with IAA for 30 min
111	GPL198	GSE3938	GSM96715	Seedling	Seedling treated with IAA for 1 hr
112	GPL198	GSE3938	GSM96715	Seedling	Seedling treated with IAA for 1 hr
113	GPL198	GSE3938	GSM96716	Seedling	Seedling treated with IAA for 3 hr
114	GPL198	GSE3938	GSM96713	Seedling	Seedling treated with Zeatin for 30 min
115	GPL198	GSE3938	GSM96713	Seedling	Seedling treated with Zeatin for 30 min
116	GPL198	GSE3938	GSM96715	Seedling	Seedling treated with Zeatin for 1 hr
117	GPL198	GSE3938	GSM96715	Seedling	Seedling treated with Zeatin for 1 hr
118	GPL198	GSE3938	GSM96716	Seedling	Seedling treated with Zeatin for 3 hr
119	GPL198	GSE3938	GSM96716	Seedling	Seedling treated with Zeatin for 3 hr
120	GPL198	GSE3938	GSM96716	Seedling	Seedling treated with Zeatin for 3 hr
121	GPL198	GSE3938	GSM96714	Seedling	Seedling treated with ABA for 30 min
122	GPL198	GSE3938	GSM96714	Seedling	Seedling treated with ABA for 30 min
123	GPL198	GSE3938	GSM96715	Seedling	Seedling treated with ABA for 1 hr
124	GPL198	GSE3938	GSM96715	Seedling	Seedling treated with ABA for 1 hr
125	GPL198	GSE3938	GSM96717	Seedling	Seedling treated with ABA for 3 hr
126	GPL198	GSE3938	GSM96717	Seedling	Seedling treated with ABA for 3 hr
127	GPL198	GSE3938	GSM96723	Seedling	Seedling treated with NPA for 3 hr
128	GPL198	GSE3938	GSM96723	Seedling	Seedling treated with NPA for 3 hr
129	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 0 hr (control)
130	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 0 hr (control)
131	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 0 hr (control)
132	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 30 min
133	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 30 min
134	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 30 min
135	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 1 hr
136	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 1 hr
137	GPL198	GSE1897	GSM46965	Seedling	Seedling treated with 1 μM IAA for 1 hr
138	GPL198	GSE1897	GSM46964	Seedling	Seedling treated with 1 μM IAA for 3 hr

Supplementary Table 4. Samples used for network analysis of *Oryza sativa* .

No.	Platform ID	Series ID	Sample ID	Sample tissue	Sample description
1	GPL2025	GSE1902	GSM470633	Stem/shoot	Stem
2	GPL2025	GSE1902	GSM470646	Stem/shoot	Stem
3	GPL2025	GSE1902	GSM470647	Stem/shoot	Stem
4	GPL2025	GSE1902	GSM470744	Stem/shoot	Stem
5	GPL2025	GSE1902	GSM470745	Stem/shoot	Stem
6	GPL2025	GSE1902	GSM470650	Stem/shoot	Stem
7	GPL2025	GSE1902	GSM470651	Stem/shoot	Stem
8	GPL2025	GSE1902	GSM470748	Stem/shoot	Stem
9	GPL2025	GSE1902	GSM470749	Stem/shoot	Stem
10	GPL2025	GSE4575	GSM1113618	Stem/shoot	Shoot
11	GPL2025	GSE4575	GSM1113622	Stem/shoot	Shoot
12	GPL2025	GSE4575	GSM1113619	Stem/shoot	Shoot
13	GPL2025	GSE4575	GSM1113623	Stem/shoot	Shoot
14	GPL2025	GSE7951	GSM195225	Stem/shoot	Shoot
15	GPL2025	GSE1902	GSM470644	Reproductive organ	Immature panicle with length between 40 and 50 mm
16	GPL2025	GSE1902	GSM470645	Reproductive organ	Immature panicle with length between 40 and 50 mm
17	GPL2025	GSE1902	GSM470742	Reproductive organ	Immature panicle with length between 40 and 50 mm
18	GPL2025	GSE1902	GSM470743	Reproductive organ	Immature panicle with length between 40 and 50 mm
19	GPL2025	GSE1902	GSM470652	Reproductive organ	Mature panicle, heading stage
20	GPL2025	GSE1902	GSM470653	Reproductive organ	Mature panicle, heading stage
21	GPL2025	GSE1902	GSM470750	Reproductive organ	Mature panicle, heading stage
22	GPL2025	GSE1902	GSM470751	Reproductive organ	Mature panicle, heading stage
23	GPL2025	GSE1902	GSM470654	Reproductive organ	Palea/lemma, just before heading date
24	GPL2025	GSE1902	GSM470655	Reproductive organ	Palea/lemma, just before heading date
25	GPL2025	GSE1902	GSM470752	Reproductive organ	Palea/lemma, just before heading date
26	GPL2025	GSE1902	GSM470753	Reproductive organ	Palea/lemma, just before heading date
27	GPL2025	GSE1902	GSM470658	Reproductive organ	Spikelet, 3 days after flowering
28	GPL2025	GSE1902	GSM470659	Reproductive organ	Spikelet, 3 days after flowering
29	GPL2025	GSE1902	GSM470756	Reproductive organ	Spikelet, 3 days after flowering
30	GPL2025	GSE1902	GSM470757	Reproductive organ	Spikelet, 3 days after flowering
31	GPL2025	GSE7951	GSM195218	Reproductive organ	Mature stigma
32	GPL2025	GSE7951	GSM195219	Reproductive organ	Mature stigma
33	GPL2025	GSE7951	GSM195220	Reproductive organ	Mature stigma
34	GPL2025	GSE7951	GSM195221	Reproductive organ	Mature ovary
35	GPL2025	GSE7951	GSM195222	Reproductive organ	Mature ovary
36	GPL2025	GSE7951	GSM195223	Reproductive organ	Mature ovary
37	GPL2025	GSE1902	GSM470656	Reproductive organ	Stamen, just before heading date
38	GPL2025	GSE1902	GSM470657	Reproductive organ	Stamen, just before heading date
39	GPL2025	GSE1902	GSM470754	Reproductive organ	Stamen, just before heading date
40	GPL2025	GSE1902	GSM470755	Reproductive organ	Stamen, just before heading date
41	GPL2025	GSE7951	GSM195227	Reproductive organ	Mature anther
42	GPL2025	GSE6893	GSM159189	Reproductive organ	Young inflorescence with length upto 3 cm
43	GPL2025	GSE6893	GSM159190	Reproductive organ	Young inflorescence with length upto 3 cm
44	GPL2025	GSE6893	GSM159191	Reproductive organ	Young inflorescence with length upto 3 cm
45	GPL2025	GSE6893	GSM159192	Reproductive organ	Inflorescence with length between 3 and 5 cm
46	GPL2025	GSE6893	GSM159193	Reproductive organ	Inflorescence with length between 3 and 5 cm
47	GPL2025	GSE6893	GSM159194	Reproductive organ	Inflorescence with length between 3 and 5 cm
48	GPL2025	GSE6893	GSM159195	Reproductive organ	Inflorescence with length between 5 and 10 cm
49	GPL2025	GSE6893	GSM159196	Reproductive organ	Inflorescence with length between 5 and 10 cm
50	GPL2025	GSE6893	GSM159197	Reproductive organ	Inflorescence with length between 5 and 10 cm
51	GPL2025	GSE6893	GSM159198	Reproductive organ	Inflorescence with length between 10 and 15 cm
52	GPL2025	GSE6893	GSM159199	Reproductive organ	Inflorescence with length between 10 and 15 cm
53	GPL2025	GSE6893	GSM159200	Reproductive organ	Inflorescence with length between 10 and 15 cm
54	GPL2025	GSE6893	GSM159201	Reproductive organ	Inflorescence with length between 15 and 22 cm
55	GPL2025	GSE6893	GSM159202	Reproductive organ	Inflorescence with length between 15 and 22 cm
56	GPL2025	GSE6893	GSM159203	Reproductive organ	Inflorescence with length between 15 and 22 cm
57	GPL2025	GSE6893	GSM159204	Reproductive organ	Inflorescence with length between 22 and 30 cm
58	GPL2025	GSE6893	GSM159205	Reproductive organ	Inflorescence with length between 22 and 30 cm
59	GPL2025	GSE6893	GSM159206	Reproductive organ	Inflorescence with length between 22 and 30 cm
60	GPL2025	GSE1902	GSM470636	Leaf	Mature leaf blade with immature panicle with less than 1 mm length
61	GPL2025	GSE1902	GSM470637	Leaf	Mature leaf blade with immature panicle with less than 1 mm length
62	GPL2025	GSE1902	GSM470734	Leaf	Mature leaf blade with immature panicle with less than 1 mm length
63	GPL2025	GSE1902	GSM470735	Leaf	Mature leaf blade with immature panicle with less than 1 mm length

Supplementary Table 4. Continued

64	GPL2025	GSE1902	GSM470638	Leaf	Mature leaf blade with immature panicle with less than 1 mm length
65	GPL2025	GSE1902	GSM470639	Leaf	Mature leaf blade with immature panicle with less than 1 mm length
66	GPL2025	GSE1902	GSM470736	Leaf	Mature leaf blade with immature panicle with less than 1 mm length
67	GPL2025	GSE1902	GSM470737	Leaf	Mature leaf blade with immature panicle with less than 1 mm length
68	GPL2025	GSE1902	GSM470640	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
69	GPL2025	GSE1902	GSM470641	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
70	GPL2025	GSE1902	GSM470738	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
71	GPL2025	GSE1902	GSM470739	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
72	GPL2025	GSE1902	GSM470642	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
73	GPL2025	GSE1902	GSM470643	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
74	GPL2025	GSE1902	GSM470740	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
75	GPL2025	GSE1902	GSM470741	Leaf	Mature leaf blade with immature panicle whith length between 40 and 50
76	GPL2025	GSE1902	GSM470648	Leaf	Flag leaf, just before heading date
77	GPL2025	GSE1902	GSM470649	Leaf	Flag leaf, just before heading date
78	GPL2025	GSE1902	GSM470746	Leaf	Flag leaf, just before heading date
79	GPL2025	GSE1902	GSM470747	Leaf	Flag leaf, just before heading date
80	GPL2025	GSE1902	GSM470666	Leaf	Flag leaf, 14 days after pollination
81	GPL2025	GSE1902	GSM470667	Leaf	Flag leaf, 14 days after pollination
82	GPL2025	GSE6893	GSM159183	Leaf	Young leaf
83	GPL2025	GSE6893	GSM159182	Leaf	Young leaf
84	GPL2025	GSE6893	GSM159184	Leaf	Young leaf
85	GPL2025	GSE6893	GSM159185	Leaf	Young leaf
86	GPL2025	GSE6893	GSM159180	Leaf	Mature leaf
87	GPL2025	GSE6893	GSM159181	Leaf	Mature leaf
88	GPL2025	GSE6893	GSM159186	Leaf	Shoot apical meristem
89	GPL2025	GSE6893	GSM159187	Leaf	Shoot apical meristem
90	GPL2025	GSE6893	GSM159188	Leaf	Shoot apical meristem
91	GPL2025	GSE6719	GSM154945	Leaf	Untreated leaf, 30 min
92	GPL2025	GSE6719	GSM154946	Leaf	Untreated leaf, 30 min
93	GPL2025	GSE6719	GSM154947	Leaf	Untreated leaf, 30 min
94	GPL2025	GSE6719	GSM154951	Leaf	Untreated leaf, 120 min
95	GPL2025	GSE6719	GSM154952	Leaf	Untreated leaf, 120 min
96	GPL2025	GSE6719	GSM154953	Leaf	Untreated leaf, 120 min
97	GPL2025	GSE6719	GSM154948	Leaf	Leaf treated with trans-Zeatin for 30 min
98	GPL2025	GSE6719	GSM154949	Leaf	Leaf treated with trans-Zeatin for 30 min
99	GPL2025	GSE6719	GSM154950	Leaf	Leaf treated with trans-Zeatin for 30 min
100	GPL2025	GSE6719	GSM154954	Leaf	Leaf treated with trans-Zeatin for 120 min
101	GPL2025	GSE6719	GSM154955	Leaf	Leaf treated with trans-Zeatin for 120 min
102	GPL2025	GSE6719	GSM154956	Leaf	Leaf treated with trans-Zeatin for 120 min
103	GPL2025	GSE5167	GSM116195	Seedling	7-day-old seedlings
104	GPL2025	GSE5167	GSM116398	Seedling	7-day-old seedlings
105	GPL2025	GSE1427	GSM357122	Seedling	14-day-old seedlings
106	GPL2025	GSE1427	GSM357133	Seedling	14-day-old seedlings
107	GPL2025	GSE1427	GSM357136	Seedling	14-day-old rice seedlings, heat shock treatment
108	GPL2025	GSE1427	GSM357137	Seedling	14-day-old rice seedlings, heat shock treatment
109	GPL2025	GSE5167	GSM116399	Seedling	Seedling treated with IAA
110	GPL2025	GSE5167	GSM116400	Seedling	Seedling treated with IAA
111	GPL2025	GSE5167	GSM116401	Seedling	Seedling treated with IAA
112	GPL2025	GSE5167	GSM116402	Seedling	Seedling treated with IAA

Supplementary Table 5. Gene used for network analysis of *Arabidopsis thaliana* and *Oryza sativa*

EC No.	Product	*Arabidopsis thaliana*		*Oryza sativa*	
		Locus name	Abbreviation in figure	Locus name	Abbreviation in figure
MVA pathway					
2.3.1.9	Acetyl-CoA acetyltransferase	At5g47720	ACAT1	LOC_Os09g07830	ACAT
		At5g48230	ACAT2		
2.3.3.10	3-Hydroxy-3-methylglutaryl CoA synthase	At4g11820	HMGCS	LOC_Os09g34960	HMGCS
1.1.1.34	3-Hydroxy-3-methylglutaryl CoA reductase	At1g76490	HMGCR1	LOC_Os09g31970	HMGCR
		At2g17370	HMGCR2		
2.7.1.36	Mevalonate kinase	At5g27450	MVK	LOC_Os10g18220	MVK
2.7.4.2	Phosphomevalonate kinase	At1g31910	PMK	LOC_Os03g14830	PMK
4.1.1.33	Diphosphomevalonate decarboxylase	At2g38700	MVD1	LOC_Os02g01920	MVD
		At3g54250	MVD2		
MEP pathway					
2.2.1.7	1-Deoxy-D-xylulose 5-phosphate synthase	At4g15560	DXPS	LOC_Os05g33840	DXPS
1.1.1.267	1-Deoxy-D-xylulose 5-phosphate reductoisomerase	At5g62790	DXR	LOC_Os01g01710	DXR
2.7.7.60	2-C-Methyl-D-erythritol 4-phosphate cytidyltransferase	At2g02500	ISPD	LOC_Os01g66360	ISPD
2.7.1.148	4-(Cytidine 5'-diphospho)-2-C-methyl-D-erythritol kinase	At2g26930	CDPMEK	LOC_Os01g58790	CDPMEK
4.6.1.12	2C-Methyl-D-erythritol 2,4-cyclodiphosphate synthase	At1g63970	ISPF	LOC_Os02g45660	ISPF
1.17.7.1	4-Hydroxy-3-methylbut-2-enyl diphosphate synthase	At5g60600	HDS	LOC_Os02g39160	HDS
1.17.1.2	4-Hydroxy-3-methylbut-2-enyl diphosphate reductase	At4g34350	HDR	LOC_Os03g52170	HDR
Isoprenyl diphospjate synthase					
5.3.3.2	Isopentenyl diphosphate isomerase	At5g16440	IDI1	LOC_Os07g36190	IDI
		At3g02780	IDI2		
	Geranylgeranyl diphosphate synthase	At4g38460	GPPS	LOC_Os02g44780	GPPS
	Farnesyl diphosphate synthase	At5g47770	FDPS1	LOC_Os01g50760	FDPS1
		At4g17190	FDPS2	LOC_Os05g46580	FDPS2
2.5.1.1, 2.5.1.10, 2.5.1.29	Geranylgeranyl pyrophosphate synthase	At4g36810	GGPPS1	LOC_Os07g39270	GGPPS
		At2g23800	GGPPS2		
		At3g14550	GGPPS3		
		At2g18640	GGPPS4		
		At1g49530	GGPPS5		
		At2g18620	GGPPS6		
		At3g14530	GGPPS7		
		At3g20160	GGPPS8		
		At3g29430	GGPPS9		
		At3g32040	GGPPS10		