**Supplementary Text S1. miRNA-target transcript validation based on degradome-seq data**

The degradome-seq data in wild-type *Arabidopsis* (Col-0) was utilized to validate the 6,093 predicted miRNA-target pairs. Firstly, clean reads of 18 degradome-seq datasets were downloaded from NCBI GEO (Supplementary Table S2). Degradome raw reads were processed to remove the adapter sequence. The kept adaptor-free reads were between 18 and 21bp length. The clean reads mapping to the Col-0 transcripts were used to identify miRNA cleavage sites by CleaveLand4 (Addo-Quaye et al., 2009). If a degradome read exactly locates at splicing site (at position 10 relative to the 5ʹ-end of miRNAs) with an obvious peak (Category 0 and 1) or is greater than the average abundance value (Category 2) of other degradome reads mapped on the transcript, this splicing site was considered reliable. Among the 6,093 miRNA-target pairs that were predicted by both TargetFinder and PsRobot, 1,229 (20.2%) pairs contain at least one reliable miRNA binding site, which were validated by degradome-seq data (Supplementary Figure S3).

**Supplementary Text S2**. **Topological and functional analysis of two complementary topological properties, hubs and bottlenecks**

Degree distribution of the miRNA–miRNA cooperative network demonstrated a power-law distribution (Supplementary Figure S5A). In other words, this network shows scale-free characteristics, indicating that most miRNAs are poorly connected and a few miRNAs connect with a relatively large number of miRNA partners. The miRNA–miRNA synergistic networks in human (Hua et al., 2014; Shao et al., 2019) and plants (Xu et al., 2014; Banerjee and Mal, 2020) also show the scale-free structure. The most highly connected miRNAs are defined as hubs, like ath-miR5658 and ath-miR5021 with the largest node size (Figure 4). In addition, a node with high node betweenness are similar to heavily used intersections in the network and called bottlenecks (Yu et al., 2007), like ath-miR5658 (also a hub) and ath-miR5641 (in gray node border, Figure 4). Hubs and bottlenecks tend to be essential nodes in the protein–protein interaction networks (Zotenko et al., 2008) and regulatory networks (Yu et al., 2007). We investigated the two complementary topological nodes in terms of topological and functional roles in the cooperative miRNA–miRNA interaction network.

Nodes with the highest degrees or the highest betweennesses are important to the stability of a network (Albert et al., 2000; Yu et al., 2007). If a node is an important mediator for network communication, removal of the node would reduce the ability of two nodes in the network to communicate, mainly due to the network interconnectedness. To compare the topological role of hubs and bottlenecks in the network, hubs and hub-nonbottlenecks were removed from the network in descending order of their degrees. Bottlenecks and nonhub-bottlenecks were removed in descending order of their betweennesses. Hub-bottlenecks and nonhub-bottlenecks were removed in descending order of their degrees first and then in descending order of their betweennesses. The impact of node removal on the network stability was estimated by main component size, which indicates the number of nodes in the largest component of the network after node deletion and is normalized by the initial size of the largest component in the network. As shown in Supplementary Figure S5B, serial deletion of hub-bottlenecks has the most significant impact on the network (yellow line). Removal of ath-miR5021 and ath-miR5658, with the highest degrees (54 and 46) and the highest node betweennesses, caused a sudden collapse in the network and the normalized main component size decreased sharply from 1 to 0.6 and then to 0.3. Nonhub-bottlenecks (cyan line) have a node deletion effect that is minor than hub-bottlenecks, but is more significant and noticeable than hub-nonbottlenecks (pink line) in the network. For example, nonhub-bottlenecks ath-miR859 and ath-miR5641 each link an interconnected subgraph with the other parts of the network. Therefore, bottlenecks tend to be more important mediators for network communication than nonbottlenecks in the cooperative miRNA–miRNA interaction network.

To further investigate the functional role of hubs and bottlenecks, we annotated each miRNA with GO biological process based on the combined set of targets co-regulated by this miRNA and its cooperative neighbors (see Materials and Methods). Supplementary Figure S5C shows that the four categories of hubs and bottlenecks regulate transcripts in many common functions, such as development (flower development, meristem development and pollen development), organ morphogenesis, regulation of programmed cell death, cell population proliferation, inorganic anion transmembrane transport, and regulation of auxin metabolic process. In addition, different categories of hubs and bottlenecks regulate some specific functions. Somatic embryogenesis and two signaling pathways are specifically regulated by the hub-nonbottlenecks in the ath-miR169 family. Nonhub-nonbottlenecks, like ath-miR165a-3p, ath-miR164b-5p, and ath-miR393b-5p, regulate some developmental process (Li and Zhang, 2016) and auxin-activated signaling pathway. Interestingly, nonhub-bottlenecks (ath-miR159a, ath-miR159b-3p, and ath-miR319c) specifically control signal transduction and plant response to gibberellin and alcohol and is also involved in the regulation of shoot system morphogenesis and vacuole organization. Obviously, miRNAs in the miRNA–miRNA cooperation network might regulate the transcripts that participate in plant developmental process, reproduction and signaling pathways.

**Supplementary Text S3. Association between the dynamic state of miRNA-target regulations and the SNP positions**

The miRNA–miRNA pairs co-regulate 10.8 transcripts on average (Supplementary Figure S4A), suggesting the function complexity of miRNA**–**miRNA cooperation. For the sd co-regulation motifs, ath-miR5021 (the general fate = KL) is cooperated with 30 miRNA partners (the general fate = K) to co-regulate 35 targets. The substitution A-to-C at position 15 of the mature sequence of ath-miR5021 leads to the drop of its regulations toward 86% (30 out of 35 targets) of its targets in the ecotypes Tscha-1 and PHW-2, while its cooperative miRNA partners keep the targets in all of the analyzed ecotypes. Besides, ath-miR5658 has two substitutions at positions 7 (A-to-C) and 17 (T-to-A), which results in the loss of regulations toward 80% (12 in 15 targets) of its targets in 46 ecotypes, while its 37 cooperative miRNAs keep these targets. For the dd co-regulation motifs, four target transcripts (AT1G40104.1, AT4G20430.1, AT4G20430.2, and AT4G20430.3) co-regulated by ath-miR394a and ath-miR394b-5p are lost in 31 ecotypes, which are associated with the SNPs within the miRNA binding sites of these transcripts.

**Supplementary Figure S1**. Climatic variables analysis. **(A)** Principal component analysis for longitude and latitude as well as the 19 climatic variables. The plot shows the quality of representation of the variables on dimensions 1 to 5 (Dim.1-5). A good representation of the variables on the principal component is positioned close to the circumference of the correlation circle. Variables that are close to the center of the plot are less important to interpret these components. **(B)** Correlation matrix of all variables. The numbers are the Pearson’s correlation coefficients between pairs of variables. Red indicates a high positive correlation, white indicates a correlation near zero, and green indicates a high negative correlation. The seven variables that were used in the study were labeled in red.

**Supplementary Figure S2**. Schematic showing four classes of nodes defined by degree and betweenness in a network. The four classes are hub-bottlenecks (blue nodes), hub-nonbottlenecks (red nodes), nonhub-bottlenecks (pink nodes), and nonhub-nonbottlenecks (green nodes). Every node in the network belongs to one of the four classes. Node size is proportional to the degree of miRNAs.

**Supplementary Figure S3**. Venn diagram of the miRNA-target transcript pairs predicted by TargetFinder (8,942 miRNA-target pairs) and PsRobot (11,415 pairs). The computational prediction results are labeled in black. The number of miRNA-target pairs validated by degradome-seq data are labeled in red.

**Supplementary Figure S4**. Variant density of mature miRNAs and their flanking regions. miRNAs were retrieved from the population-level miRNA-target regulation dataset. miRNAs were classified into conserved (red bar) and non-conserved ones (blue bar). Variant density indicates the number of SNPs and small indels per kb region. In addition to the average variant density in miRNA regions, the average variant densitie in their 5 kb upstream and downstream regions were calculated. The error bar indicates standard error of the mean. The difference of variant density between miRNAs and their flanking regions were assessed using the Analysis of Variance (ANOVA) with the TukeyHSD post-hoc method. Benjamini and Hochberg correction was applied for multiple hypothesis testing. The symbol \* denotes *P*-value < 0.01, and \*\* denotes *P*-value < 0.001.

**Supplementary Figure S5**. Relationship between miRNA-miRNA pairs and their common target transcripts. (**A**) The histogram of cooperative miRNA pairs according to the number of common target transcripts. (**B**) The histogram of transcripts according to the number of miRNA*i*-miRNA*j*-target*t* coregulation motifs.

**Supplementary Figure S6.** Topological and functional roles of the hubs and bottlenecks. (**A**) Degree distribution of the miRNA–miRNA cooperation network. Degree (*k*) is the number of connections to each miRNA. P(*k*) indicates the proportion of nodes having *k* connections. The distribution shows this network follows power-law degree distribution (dotted line) and has scale-free topology. Law’s exponent (γ) and coefficient (R-square) were labeled beside the line. (**B**) miRNA–miRNA cooperative network tolerance to the serial deletion of hubs and bottlenecks. Nodes in the network were divided into four classes: hub-bottlenecks (HBs, yellow line), nonhub-bottlenecks (NH-Bs, cyan line), hub-nonbottlenecks (H-NBs, pink line) and nonhub-nonbottlenecks (NH-NBs, gray line). The x-axis indicates the proportion of deleted nodes in all nodes of the miRNA–miRNA cooperative network. The impact of node deletion is quantified by the main component size which is the size of the remaining largest component and is normalized by the initial size of the largest component in the miRNA–miRNA cooperative network. (**C**) GO biological process categories regulated by hub-bottlenecks, nonhub-bottlenecks, hub-nonbottlenecks and nonhub-nonbottlenecks. The bar on the right represents GO biological process categories regulated by at least two classes of nodes, and the bar on the left represents GO biological process categories regulated by only one node class. The length of the bars shows the percentage of annotated nodes among all nodes within a certain class.

**Supplementary Figure S7**. Density of the expression correlation coefficients over (**A**) the conserved and conserved miRNA–miRNA pairs, (**B**) the non-conserved and non-conserved pairs as well as (**C**) the non-conserved and conserved pairs in the ‘final‘, ‘deleted‘ and ‘random‘ datasets.

**Supplementary Figure S8**. Distribution of the observed SS, DD, and SD miRNA–miRNA pairs in different conservation groups. miRNAs are classified into conserved (CS) group and non-conserved (non-CS) group.

**Supplementary Figure S9**. An example of two SD miRNA pairs, one between ath-miR838 and ath-miR156j, and the other between ath-miR838 and ath-miR156h, act as bridges (dotted orange lines) to link two inter-connected subgraph clusters.

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