# Supplementary information

# Three TF Co-expression Modules Regulate Pressure-Overload Cardiac Hypertrophy in Male Mice

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**Supplementary Table S1.** Overrepresented similar groups of GO terms for differentially expressed (DE) genes generated by Gorilla and REVIGO. BP, MF, and CC represent the GO categories of biological process, molecular function, and cellular component, respectively.

| GO term ID (BP) | Description | $\log_{10}$(*p*-value) |
|---|---|---|
| GO:0007606 | sensory perception of chemical stimulus | -15.87 |
| GO:0007186 | G-protein coupled receptor signaling pathway | -13.45 |
| GO:0006952 | defense response | -9.71 |
| GO:0022610 | biological adhesion | -9.31 |
| GO:0007155 | cell adhesion | -8.93 |
| GO:0002684 | positive regulation of immune system process | -8.82 |
| GO:0002376 | immune system process | -8.16 |
| GO:0003008 | system process | -7.16 |
| GO:0051606 | detection of stimulus | -7 |
| GO:0060326 | cell chemotaxis | -6.5 |
| GO:0010466 | negative regulation of peptidase activity | -5.6 |
| GO:0044707 | single-multicellular organism process | -5.45 |
| GO:0051240 | positive regulation of multicellular organismal process | -5.32 |
| GO:0032501 | multicellular organismal process | -5.18 |
| GO:0030001 | metal ion transport | -5.15 |
| GO:0070098 | chemokine-mediated signaling pathway | -4.88 |
| GO:0030198 | extracellular matrix organization | -4.8 |
| GO:0043062 | extracellular structure organization | -4.72 |
| GO:0048520 | positive regulation of behavior | -4.58 |
| GO:0050896 | response to stimulus | -4.44 |
| GO:0008284 | positive regulation of cell proliferation | -4 |
| GO:0031341 | regulation of cell killing | -3.5 |

| GO term ID (MF) | Description | $\log_{10}$(*p*-value) |
|---|---|---|
| GO:0004872 | receptor activity | -12.44 |
| GO:0004984 | olfactory receptor activity | -11.56 |
| GO:0005539 | glycosaminoglycan binding | -11.38 |
| GO:0008201 | heparin binding | -9.63 |
| GO:0060089 | molecular transducer activity | -9.42 |
| GO:0005216 | ion channel activity | -8.12 |
| GO:0005125 | cytokine activity | -7.28 |
| GO:0005201 | extracellular matrix structural constituent | -6.69 |
| GO:0030414 | peptidase inhibitor activity | -6.56 |

| | | |
|---|---|---|
| GO:1901681 | sulfur compound binding | -4.5 |
| GO:0001968 | fibronectin binding | -3.45 |

| **GO term ID (CC)** | **Description** | **$\log_{10}$(*p*-value)** |
|---|---|---|
| GO:0005576 | extracellular region | -31.6 |
| GO:0005578 | proteinaceous extracellular matrix | -16.29 |
| GO:0031012 | extracellular matrix | -16.21 |
| GO:0005887 | integral component of plasma membrane | -10.29 |
| GO:0005581 | collagen trimer | -8.02 |
| GO:0044459 | plasma membrane part | -7.83 |
| GO:0016021 | integral component of membrane | -7.75 |
| GO:0044298 | cell body membrane | -3.6 |
| GO:0044425 | membrane part | -4 |

# Supplementary Figures

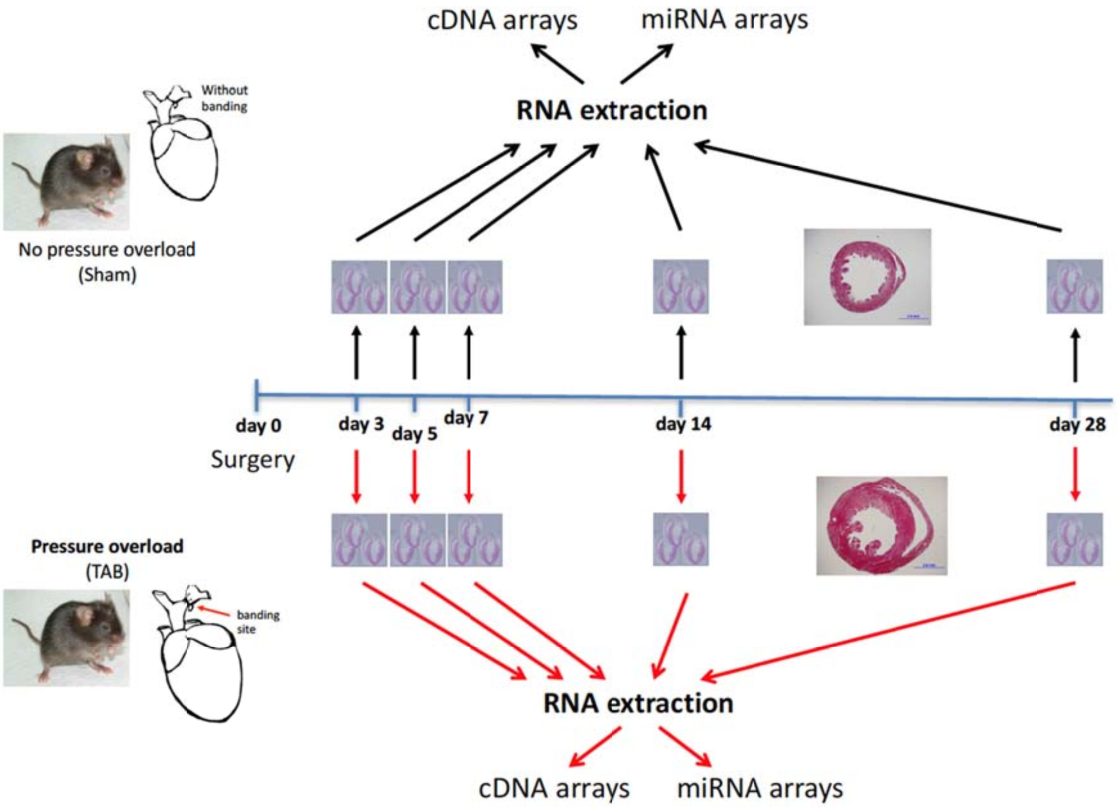


**Figure S1**. Design of the experiment. Eight-week-old adult male mice were subjected to pressure overload by transverse aortic banding (TAB). The RNAs of cardiac tissues were taken from mice subjected to TAB or sham operation at days 3, 5, 7, 14, and 28 after surgery. The expression level changes of mRNAs and miRNAs were measured by cDNA and miRNA microarrays, respectively.

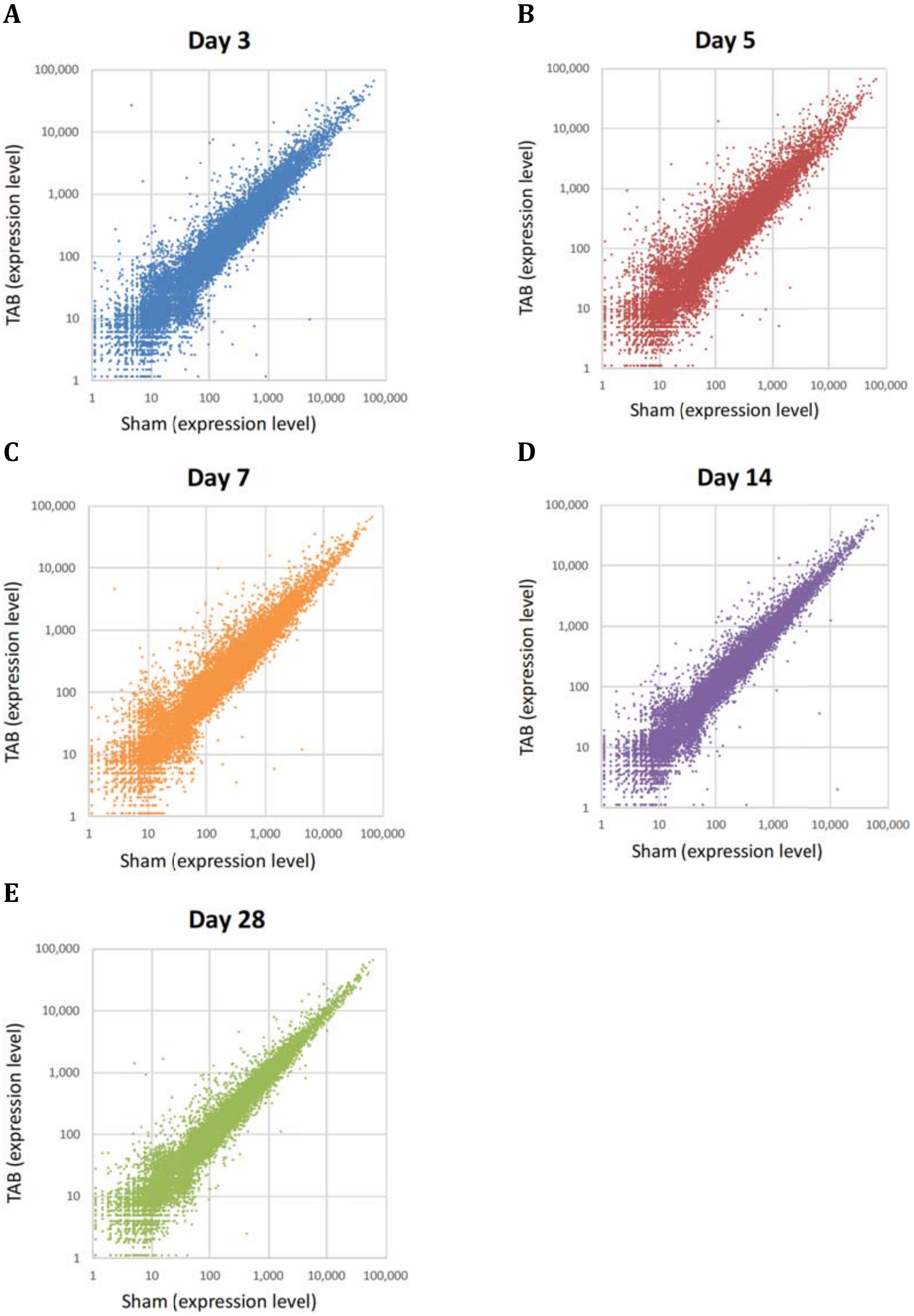


**Figure S2.** Scatter plots of TAB vs. sham gene expression levels at the five time points: (A) Day 3, (B) Day 5, (C) Day 7, (D) Day 14, and (E) Day 28. Each dot in the plot represents a gene with expression levels in sham (x-axis) and TAB (y-axis) conditions.

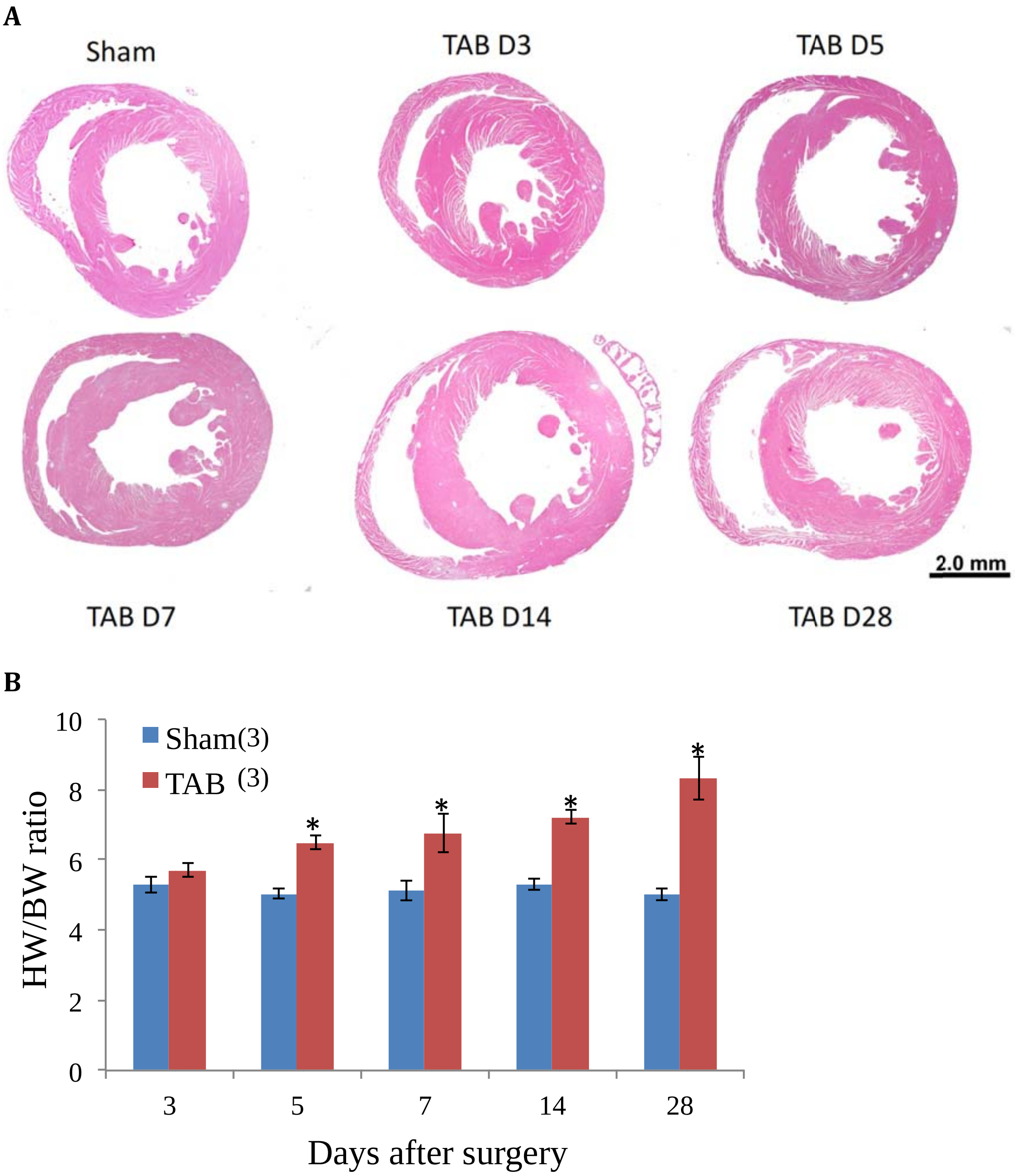


**Figure S3.** The cardiac hypertrophy in mice after TAB surgery. (A) Anatomic pictures of heart hypertrophy at different time points. (B) Heart weight/body weight (HW/BW) ratio of mice subjected to sham or TAB surgery after different time points. N=3 in each group, *$p<0.05$ when compare to sham group.

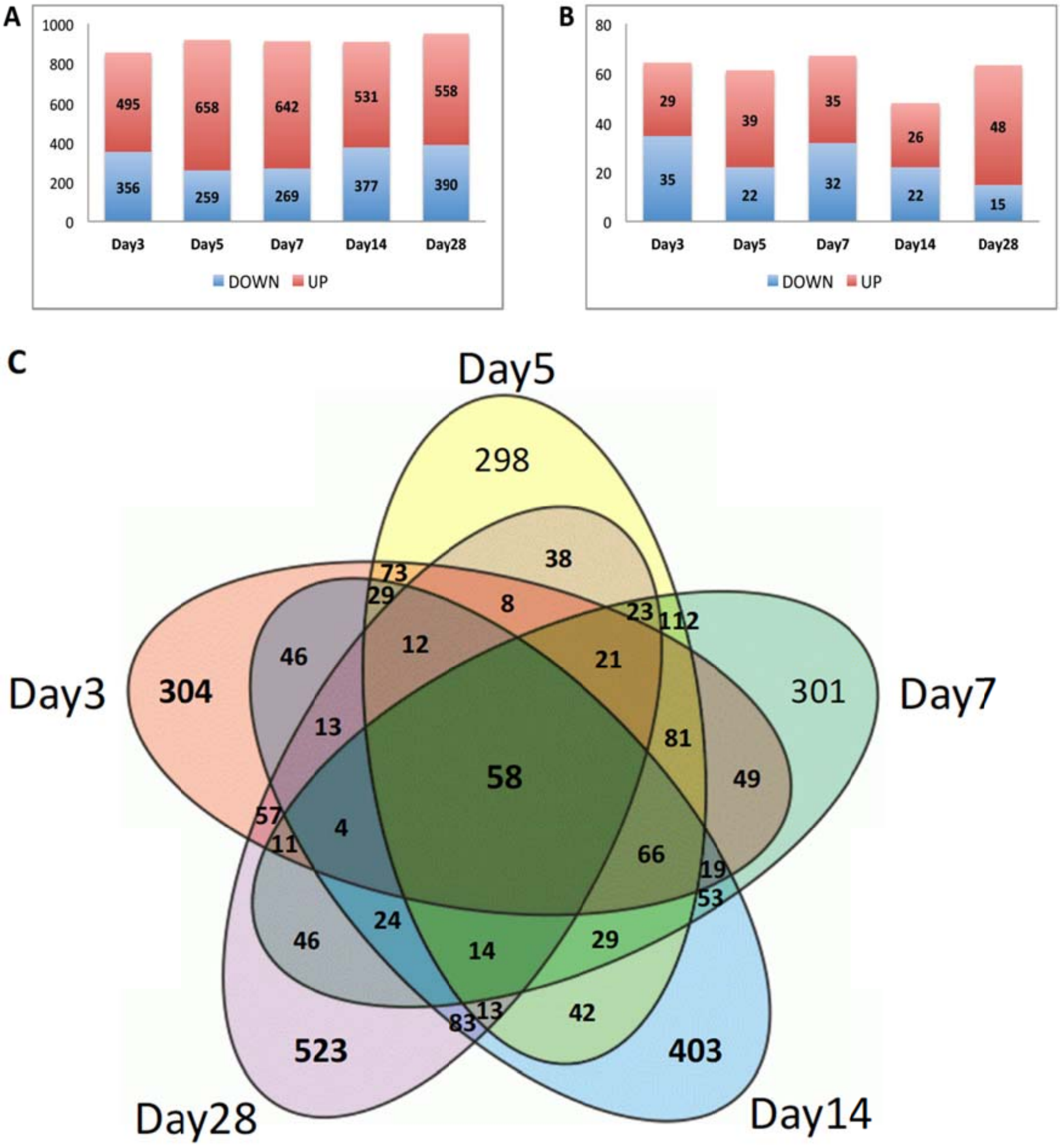


**Figure S4.** Numbers of differentially expressed (DE) genes and miRNAs at different time points. (A) Numbers of up- (red bars) and down-regulated (blue bars) DE genes at five time points. (B) Numbers of up- (red bars) and down-regulated (blue bars) DE miRNAs at five time points. (C) A Venn diagram to show the number of DE genes at five time points.

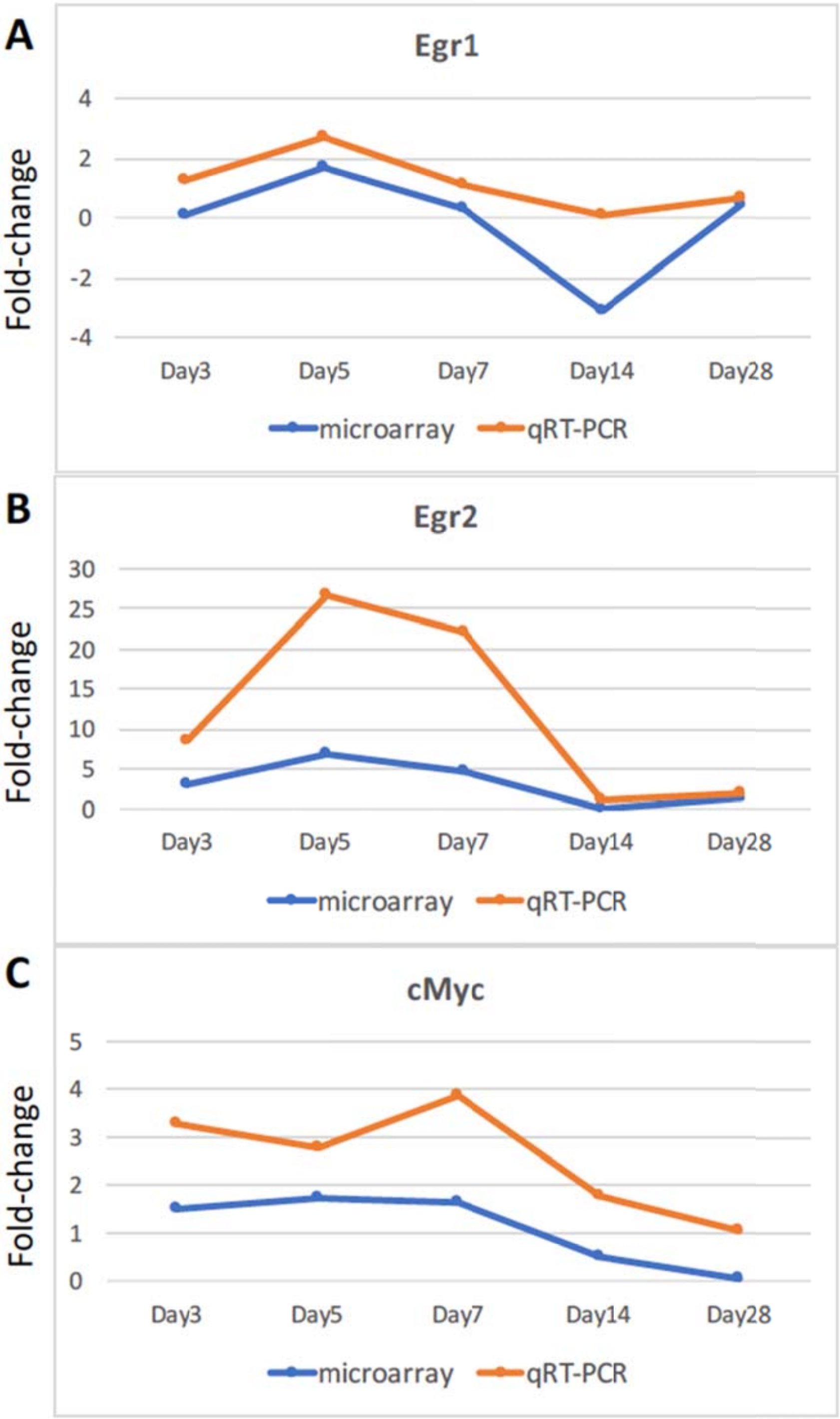


**Figure S5.** Fold-changes from expression levels comparing TAB and sham conditions for (A) *Egr1*, (B) *Egr2*, and (C) *cMyc*.

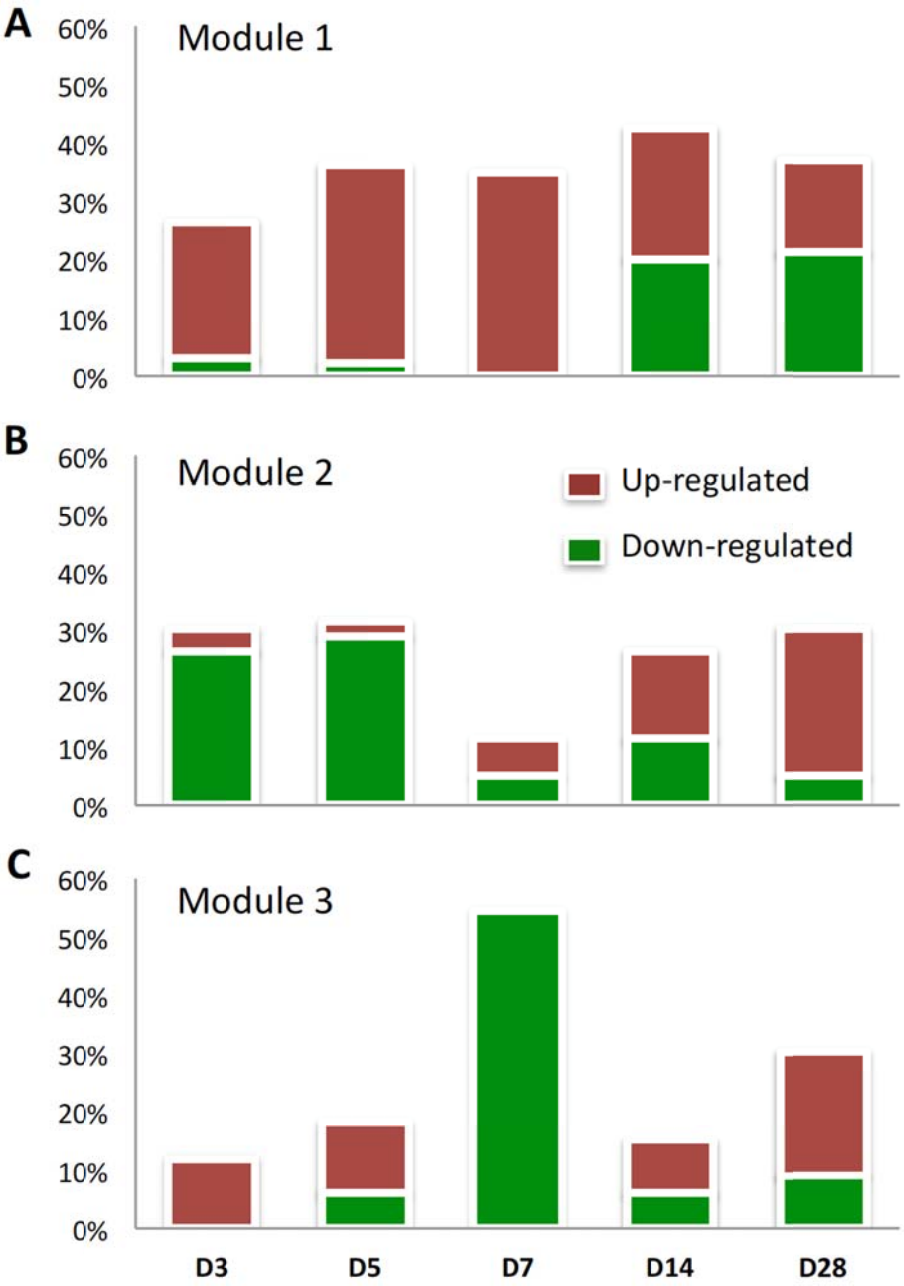
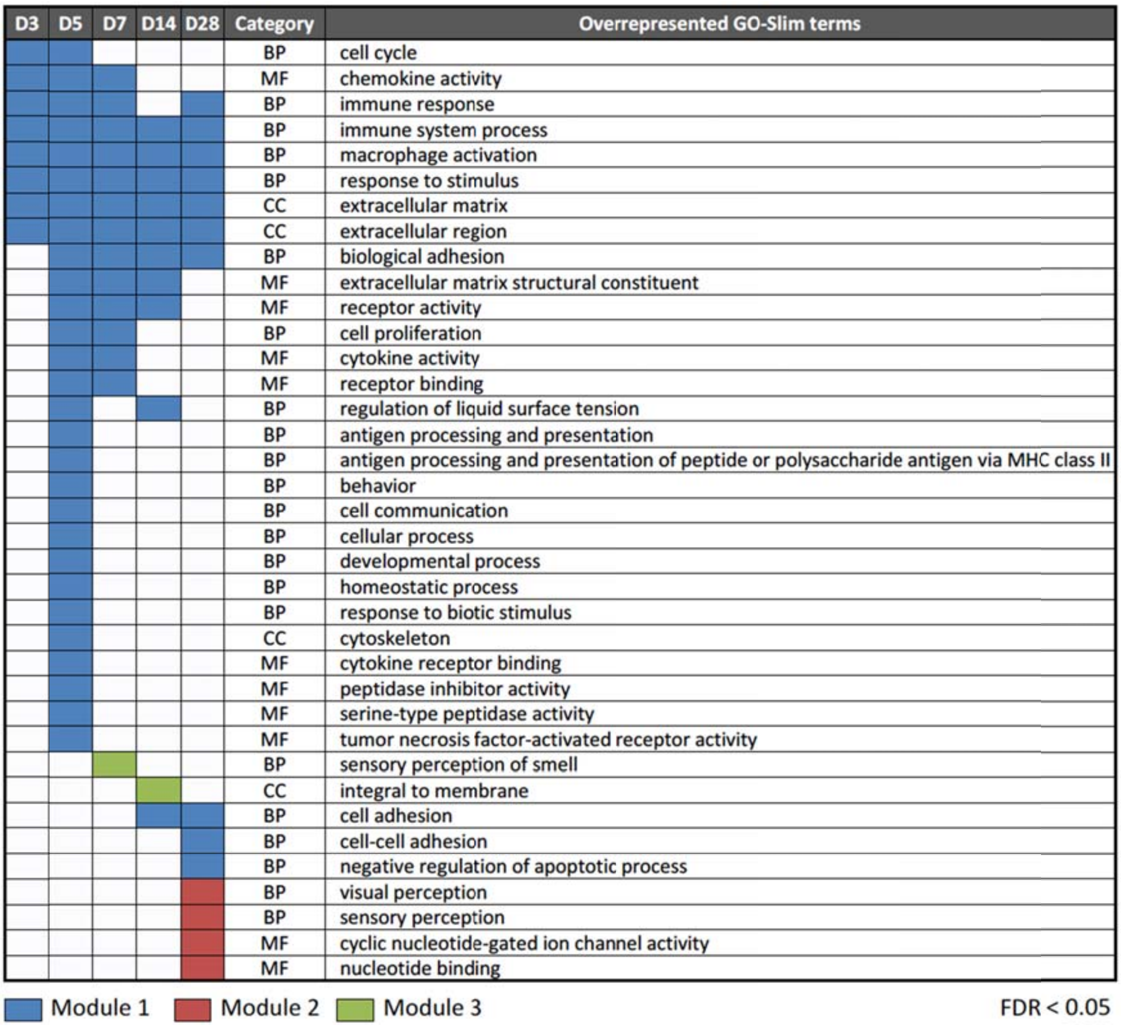


**Figure S6.** Proportions of up- and down-regulated DE TF genes in the three TF gene co-expression modules at five time points. (A) 94 TF genes in the Module 1, (B) 79 TF genes in the Module 2, and (C) 33 TF genes in the Module 3.



| D3 | D5 | D7 | D14 | D28 | Category | Overrepresented GO-Slim terms |
|---|---|---|---|---|---|---|
| 🟦 | 🟦 | | | | BP | cell cycle |
| 🟦 | 🟦 | 🟦 | | | MF | chemokine activity |
| 🟦 | 🟦 | 🟦 | | 🟦 | BP | immune response |
| 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | BP | immune system process |
| 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | BP | macrophage activation |
| 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | BP | response to stimulus |
| 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | CC | extracellular matrix |
| 🟦 | 🟦 | 🟦 | 🟦 | 🟦 | CC | extracellular region |
| | 🟦 | 🟦 | 🟦 | 🟦 | BP | biological adhesion |
| | 🟦 | 🟦 | 🟦 | | MF | extracellular matrix structural constituent |
| | 🟦 | 🟦 | 🟦 | | MF | receptor activity |
| | 🟦 | 🟦 | | | BP | cell proliferation |
| | 🟦 | 🟦 | | | MF | cytokine activity |
| | 🟦 | 🟦 | | | MF | receptor binding |
| | 🟦 | | 🟦 | | BP | regulation of liquid surface tension |
| | 🟦 | | | | BP | antigen processing and presentation |
| | 🟦 | | | | BP | antigen processing and presentation of peptide or polysaccharide antigen via MHC class II |
| | 🟦 | | | | BP | behavior |
| | 🟦 | | | | BP | cell communication |
| | 🟦 | | | | BP | cellular process |
| | 🟦 | | | | BP | developmental process |
| | 🟦 | | | | BP | homeostatic process |
| | 🟦 | | | | BP | response to biotic stimulus |
| | 🟦 | | | | CC | cytoskeleton |
| | 🟦 | | | | MF | cytokine receptor binding |
| | 🟦 | | | | MF | peptidase inhibitor activity |
| | 🟦 | | | | MF | serine-type peptidase activity |
| | 🟦 | | | | MF | tumor necrosis factor-activated receptor activity |
| | | 🟩 | | | BP | sensory perception of smell |
| | | | 🟩 | | CC | integral to membrane |
| | | | 🟦 | 🟦 | BP | cell adhesion |
| | | | | 🟦 | BP | cell-cell adhesion |
| | | | | 🟦 | BP | negative regulation of apoptotic process |
| | | | | 🟥 | BP | visual perception |
| | | | | 🟥 | BP | sensory perception |
| | | | | 🟥 | MF | cyclic nucleotide-gated ion channel activity |
| | | | | 🟥 | MF | nucleotide binding |

🟦 Module 1 🟥 Module 2 🟩 Module 3 FDR < 0.05

**Figure S7.** GO-Slim enrichment analysis for genes coexpressed with DE TF genes of the three modules at five time points. The columns on the left represent the time points. The rows represent the GO-Slim terms. We used blue, red, and green to indicate Modules 1, 2, and 3 in the GCN (Fig. 3A), respectively. The colored boxes represent the GO-Slim term of the row that is enriched at that time point of the column for genes coexpressed with DE TF genes in the module.

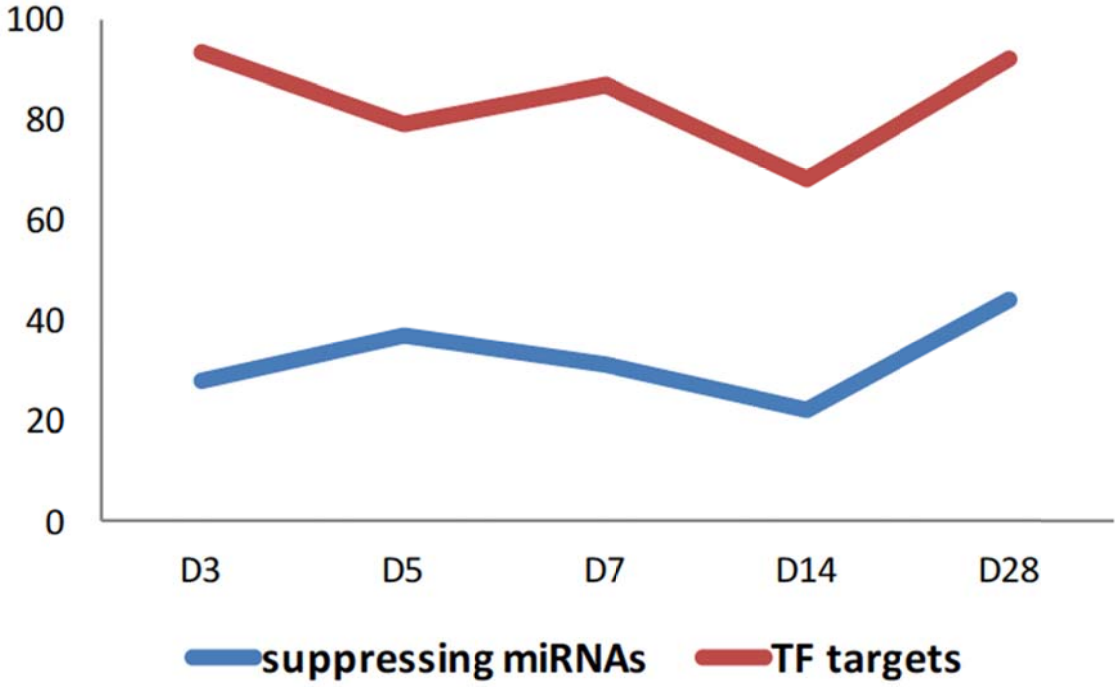


**Figure S8.** Numbers of suppressing miRNAs and suppressed TF gene targets of the three modules at five time points.