**Supplemental data**

**Supplemental tables**

**Table S1. Summary statistics for RNA sequencing data**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **#** | **Time** | **Sample Name** | **Raw data** | **After filtering (%)** | **Mapped reads (%)** | **Uniquely mapped reads (%)** | **Ensembl 77 (26,689 coding genes)** | |
| **Expressed genes (FPKM > 0)** | **Unexpressed genes** |
| 1 | 1 hour | CN-1H-037 | 42,639,278 | 40,725,078 (95.51%) | 39,473,500 (92.58%) | 37,148,046 (87.12%) | 16,855 | 9,834 |
| 2 | CN-1H-039 | 42,870,546 | 40,870,846 (95.34%) | 39,563,592 (92.29%) | 37,390,250 (87.22%) | 16,879 | 9,810 |
| 3 | CN-1H-040 | 46,738,936 | 44,583,224 (95.39%) | 42,988,890 (91.98%) | 40,624,866 (86.92%) | 17,029 | 9,660 |
| 4 | SH-1H-041 | 45,722,064 | 43,267,116 (94.63%) | 41,678,246 (91.16%) | 39,414,134 (86.20%) | 16,847 | 9,842 |
| 5 | SH-1H-042 | 58,413,588 | 55,450,384 (94.93%) | 53,004,670 (90.74%) | 50,219,034 (85.97%) | 17,346 | 9,343 |
| 6 | SH-1H-043 | 63,953,456 | 60,638,834 (94.82%) | 58,119,522 (90.88%) | 53,190,452 (83.17%) | 17,512 | 9,177 |
| 7 | 1 day | CN-1D-011 | 46,746,568 | 44,859,582 (95.96%) | 42,549,530 (91.02%) | 39,984,544 (85.53%) | 16,344 | 10,345 |
| 8 | CN-1D-013 | 43,865,624 | 41,291,262 (94.13%) | 39,476,544 (89.99%) | 37,074,150 (84.52%) | 16,624 | 10,065 |
| 9 | CN-1D-015 | 49,903,874 | 46,973,068 (94.13%) | 44,983,870 (90.14%) | 41,996,478 (84.15%) | 16,795 | 9,894 |
| 10 | SH-1D-018 | 42,495,270 | 40,209,492 (94.62%) | 38,446,360 (90.47%) | 36,336,646 (85.51%) | 16,706 | 9,983 |
| 11 | SH-1D-019 | 50,855,336 | 48,182,582 (94.74%) | 46,218,882 (90.88%) | 43,602,554 (85.74%) | 16,871 | 9,818 |
| 12 | SH-1D-020 | 45,213,260 | 42,448,724 (93.89%) | 40,523,164 (89.63%) | 38,431,132 (85.00%) | 16,570 | 10,119 |
| 13 | 1 week | CN-1W-003 | 44,905,068 | 43,034,698 (95.83%) | 41,105,910 (91.54%) | 38,677,366 (86.13%) | 16,992 | 9,697 |
| 14 | CN-1W-004 | 40,119,532 | 38,560,118 (96.11%) | 36,898,844 (91.97%) | 34,393,116 (85.73%) | 15,981 | 10,708 |
| 15 | CN-1W-005 | 45,502,482 | 43,802,238 (96.26%) | 42,120,892 (92.57%) | 39,419,112 (86.63%) | 16,421 | 10,268 |
| 16 | SH-1W-007 | 50,339,306 | 48,281,798 (95.91%) | 46,095,768 (91.57%) | 43,476,992 (86.37%) | 15,963 | 10,726 |
| 17 | SH-1W-009 | 38,859,972 | 37,459,550 (96.40%) | 35,711,954 (91.90%) | 33,791,842 (86.96%) | 16,042 | 10,647 |
| 18 | SH-1W-010 | 47,452,532 | 45,477,376 (95.84%) | 43,535,248 (91.74%) | 41,200,106 (86.82%) | 16,657 | 10,032 |
| 19 | 1 month | CN-1M-026 | 55,402,064 | 52,607,258 (94.96%) | 49,107,832 (88.64%) | 45,077,902 (81.37%) | 17,285 | 9,404 |
| 20 | CN-1M-028 | 41,733,322 | 39,745,926 (95.24%) | 38,653,110 (92.62%) | 36,052,120 (86.39%) | 16,789 | 9,900 |
| 21 | CN-1M-029 | 50,330,958 | 47,725,414 (94.82%) | 45,151,232 (89.71%) | 42,276,934 (84.00%) | 17,259 | 9,430 |
| 22 | SH-1M-032 | 39,958,202 | 38,097,978 (95.34%) | 36,761,140 (92.00%) | 34,750,316 (86.97%) | 16,728 | 9,961 |
| 23 | SH-1M-034 | 42,977,764 | 40,962,526 (95.31%) | 39,455,278 (91.80%) | 37,311,198 (86.82%) | 16,867 | 9,822 |
| 24 | SH-1M-035 | 46,314,350 | 44,159,808 (95.35%) | 42,712,286 (92.22%) | 40,249,750 (86.91%) | 16,861 | 9,828 |
| 25 | 3 month | CN-3M-011 | 46,654,358 | 43,090,012 (92.36%) | 41,521,360 (89.00%) | 39,191,094 (84.00%) | 17,249 | 9,440 |
| 26 | CN-3M-012 | 47,296,366 | 43,667,658 (92.33%) | 42,071,446 (88.95%) | 39,768,200 (84.08%) | 17,209 | 9,480 |
| 27 | CN-3M-026 | 48,960,598 | 45,011,254 (91.93%) | 43,422,062 (88.69%) | 40,928,042 (83.59%) | 17,204 | 9,485 |
| 28 | SH-3M-020 | 47,199,010 | 43,417,268 (91.99%) | 41,758,296 (88.47%) | 39,605,534 (83.91%) | 16,988 | 9,701 |
| 29 | SH-3M-022 | 40,255,992 | 37,077,584 (92.10%) | 35,673,884 (88.62%) | 33,850,032 (84.09%) | 16,715 | 9,974 |
| 30 | SH-3M-024 | 41,104,274 | 38,255,026 (93.07%) | 36,843,292 (89.63%) | 34,914,430 (84.94%) | 16,701 | 9,988 |

**Table S2. Results of the expressed genes in all samples**

|  |  |
| --- | --- |
| Category | Number of genes |
| Total genes in database | 26,689 |
| Undetected genes | 6,502 |
| Expressed genes in all samples | 20,187 |
| At least one sample | 19,812 |
| Commonly expressed genes in all samples | 14,370 |

**Table S3.** **Lists of featured functions of gene ontology (GO) biological processes at 5 time points obtained using Metascape software**

**(A) 1 hour**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Term** | **Description** | **LogP** | **Log**  **(q-value)** | **InTerm\_ InList** |
| GO:0006954 | inflammatory response | -22.29660673 | -17.947 | 36/457 |
| GO:0010942 | positive regulation of cell death | -16.10973648 | -12.362 | 36/705 |
| GO:0001817 | regulation of cytokine production | -15.90176566 | -12.251 | 37/760 |
| GO:0019221 | cytokine-mediated signaling pathway | -15.46872242 | -11.897 | 25/316 |
| GO:1903037 | regulation of leukocyte cell–cell adhesion | -14.93619943 | -11.432 | 25/333 |
| GO:0001228 | DNA-binding transcription activator activity, RNA polymerase II-specific | -14.00840399 | -10.773 | 28/476 |
| GO:0000302 | response to reactive oxygen species | -13.78837565 | -10.615 | 21/243 |
| GO:1901652 | response to peptide | -13.36017774 | -10.333 | 31/632 |
| GO:0009611 | response to wounding | -13.17777865 | -10.208 | 28/514 |
| GO:1902105 | regulation of leukocyte differentiation | -12.47283397 | -9.634 | 22/317 |
| GO:0031960 | response to corticosteroid | -12.14767286 | -9.358 | 22/329 |
| GO:0032652 | regulation of interleukin-1 production | -11.5132951 | -8.863 | 14/112 |
| GO:0051090 | regulation of DNA-binding transcription factor activity | -11.34618064 | -8.735 | 24/439 |
| GO:0009991 | response to extracellular stimulus | -11.34413634 | -8.735 | 31/754 |
| GO:0015671 | oxygen transport | -10.42755604 | -7.891 | 7/15 |
| GO:0009314 | response to radiation | -9.438478109 | -7.033 | 24/543 |
| GO:0002520 | immune system development | -9.422237054 | -7.027 | 29/792 |
| GO:0001944 | vasculature development | -9.40630636 | -7.016 | 24/545 |
| GO:0006915 | apoptotic process | -8.927479543 | -6.599 | 27/726 |
| GO:0031099 | regeneration | -8.873587079 | -6.549 | 17/278 |

**(B) 1 day**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Term** | **Description** | **LogP** | **Log**  **(q-value)** | **InTerm\_ InList** |
| GO:0006954 | inflammatory response | -22.53753301 | -18.188 | 55/457 |
| GO:0099699 | integral component of synaptic membrane | -17.73170632 | -13.683 | 29/233 |
| GO:0009611 | response to wounding | -14.49620505 | -10.925 | 47/514 |
| GO:0046873 | metal ion transmembrane transporter activity | -14.28047271 | -10.776 | 33/414 |
| GO:0007610 | behavior | -13.72061144 | -10.371 | 43/735 |
| GO:0031099 | regeneration | -13.43823208 | -10.168 | 33/278 |
| GO:0030335 | positive regulation of cell migration | -13.39012439 | -10.155 | 49/593 |
| GO:0010942 | positive regulation of cell death | -12.80458541 | -9.723 | 53/705 |
| GO:0099056 | integral component of presynaptic membrane | -12.52462105 | -9.573 | 18/121 |
| GO:0071621 | granulocyte chemotaxis | -12.24019765 | -9.338 | 18/81 |
| GO:0045765 | regulation of angiogenesis | -11.49104354 | -8.754 | 32/307 |
| GO:0009612 | response to mechanical stimulus | -10.90822245 | -7.152 | 43/341 |
| GO:0048545 | response to steroid hormone | -10.56306836 | -7.962 | 38/456 |
| GO:0015081 | sodium ion transmembrane transporter activity | -10.3060203 | -7.727 | 17/142 |
| GO:0070555 | response to interleukin-1 | -10.02166748 | -7.465 | 22/167 |
| GO:0002685 | regulation of leukocyte migration | -10.00676373 | -7.463 | 26/235 |
| GO:0002683 | negative regulation of immune system process | -9.973568299 | -7.437 | 36/434 |
| GO:0032355 | response to estradiol | -9.299047024 | -5.950 | 34/257 |
| GO:0001818 | negative regulation of cytokine production | -9.275757837 | -6.821 | 28/292 |
| GO:0007268 | chemical synaptic transmission | -9.267909957 | -6.821 | 25/374 |

**(C) 1 week**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Term** | **Description** | **LogP** | **Log(q-value)** | **InTerm\_InList** |
| GO:0001775 | cell activation | -39.84991 | -35.500 | 137/671 |
| GO:0001817 | regulation of cytokine production | -34.27252 | -30.400 | 138/760 |
| GO:0031347 | regulation of defense response | -33.05142 | -29.304 | 120/611 |
| GO:0006954 | inflammatory response | -32.90777 | -29.257 | 102/457 |
| GO:0045087 | innate immune response | -32.06855 | -28.497 | 112/553 |
| GO:0050865 | regulation of cell activation | -31.95431 | -28.450 | 122/645 |
| GO:0002252 | immune effector process | -30.56635 | -27.120 | 83/331 |
| GO:0050778 | positive regulation of immune response | -27.40696 | -24.099 | 99/501 |
| GO:0098793 | presynapse | -27.2313 | -23.961 | 68/669 |
| GO:0030335 | positive regulation of cell migration | -26.17612 | -23.003 | 107/593 |
| GO:0002697 | regulation of immune effector process | -24.43718 | -21.410 | 84/409 |
| GO:0009897 | external side of plasma membrane | -23.46181 | -20.474 | 88/458 |
| GO:0050764 | regulation of phagocytosis | -21.7232 | -18.821 | 42/120 |
| GO:0016126 | sterol biosynthetic process | -20.88241 | -18.010 | 19/41 |
| GO:0009615 | response to virus | -19.20185 | -16.454 | 62/288 |
| GO:0002250 | adaptive immune response | -18.41919 | -15.713 | 57/256 |
| GO:0019221 | cytokine-mediated signaling pathway | -18.35694 | -15.661 | 64/316 |
| GO:0097060 | synaptic membrane | -17.78238 | -15.132 | 46/466 |
| GO:0043025 | neuronal cell body | -17.62759 | -15.002 | 59/763 |
| GO:1902105 | regulation of leukocyte differentiation | -16.38948 | -13.860 | 61/317 |

**(D) 1 month**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Term** | **Description** | **LogP** | **Log(q-value)** | **InTerm\_InList** |
| GO:0098793 | presynapse | -62.0390898 | -57.690 | 119/669 |
| GO:0097060 | synaptic membrane | -52.3536929 | -48.305 | 93/466 |
| GO:0001775 | cell activation | -39.94299004 | -36.439 | 123/671 |
| GO:0022626 | cytosolic ribosome | -36.92594037 | -33.690 | 56/141 |
| GO:0045087 | innate immune response | -35.3321433 | -32.129 | 105/553 |
| GO:0042391 | regulation of membrane potential | -33.05973081 | -29.965 | 74/485 |
| GO:0050804 | modulation of chemical synaptic transmission | -31.36439972 | -28.337 | 83/651 |
| GO:0002252 | immune effector process | -29.55846135 | -26.624 | 74/331 |
| GO:0050778 | positive regulation of immune response | -27.62356153 | -24.765 | 89/501 |
| GO:0031347 | regulation of defense response | -27.44806501 | -24.604 | 99/611 |
| GO:0043025 | neuronal cell body | -27.15171712 | -24.321 | 84/763 |
| GO:0006954 | inflammatory response | -26.43179787 | -23.650 | 83/457 |
| GO:0001817 | regulation of cytokine production | -26.22924973 | -23.460 | 110/760 |
| GO:0050865 | regulation of cell activation | -25.55200391 | -22.836 | 99/645 |
| GO:0060627 | regulation of vesicle-mediated transport | -23.87086154 | -20.220 | 124/623 |
| GO:0009615 | response to virus | -23.84330777 | -21.184 | 62/288 |
| GO:0050808 | synapse organization | -22.95202474 | -20.373 | 51/330 |
| GO:0098552 | side of membrane | -22.78449848 | -20.227 | 97/676 |
| GO:0002683 | negative regulation of immune system process | -22.5000347 | -19.957 | 75/434 |
| GO:0043269 | regulation of ion transport | -21.87365411 | -19.350 | 76/760 |

**(E) 3 months**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Term** | **Description** | **LogP** | **Log(q-value)** | **InTerm\_InList** |
| GO:0001775 | cell activation | -46.63073609 | -42.281 | 131/671 |
| GO:0050865 | regulation of cell activation | -36.71654036 | -32.844 | 115/645 |
| GO:0002252 | immune effector process | -35.8902744 | -32.143 | 81/331 |
| GO:0045087 | innate immune response | -35.21334784 | -31.563 | 104/553 |
| GO:0050778 | positive regulation of immune response | -30.23733231 | -26.733 | 92/501 |
| GO:0002683 | negative regulation of immune system process | -29.26873353 | -25.836 | 84/434 |
| GO:0001817 | regulation of cytokine production | -29.23134256 | -25.836 | 114/760 |
| GO:0006954 | inflammatory response | -28.32290178 | -24.973 | 85/457 |
| GO:0031347 | regulation of defense response | -27.99543943 | -24.687 | 99/611 |
| GO:0032103 | positive regulation of response to external stimulus | -27.59804355 | -24.362 | 83/447 |
| GO:0002250 | adaptive immune response | -25.51057045 | -22.337 | 60/256 |
| GO:0016126 | sterol biosynthetic process | -25.0192988 | -21.874 | 18/41 |
| GO:0009897 | external side of plasma membrane | -24.76157213 | -21.643 | 80/458 |
| GO:0030335 | positive regulation of cell migration | -23.32931051 | -20.343 | 90/593 |
| GO:0098793 | presynapse | -22.93455192 | -20.016 | 44/669 |
| GO:0097060 | synaptic membrane | -20.94358944 | -18.114 | 36/466 |
| GO:0002274 | myeloid leukocyte activation | -20.24152864 | -17.483 | 41/150 |
| GO:0050764 | regulation of phagocytosis | -19.32446301 | -16.647 | 36/120 |
| GO:0009611 | response to wounding | -19.00825676 | -16.358 | 76/514 |
| GO:0002764 | immune response-regulating signaling pathway | -18.41727776 | -15.800 | 51/256 |

**Table S4. Normalized expression FPKM values and statistical information for 2,841 DEGs**

Data available at <https://www.dropbox.com/s/n119ai77ag3iv0i/Supplementary%20Table%20S4_2841DEGs.xlsx?dl=0>

**Table S5. Detailed information for DPGP clustering modules**

Data available at <https://www.dropbox.com/s/thbqgrg8qziy9ma/Supplementary%20Table%20S5_DPGP%20clusted%20module%20DEGs_4_parts.xlsx?dl=0>

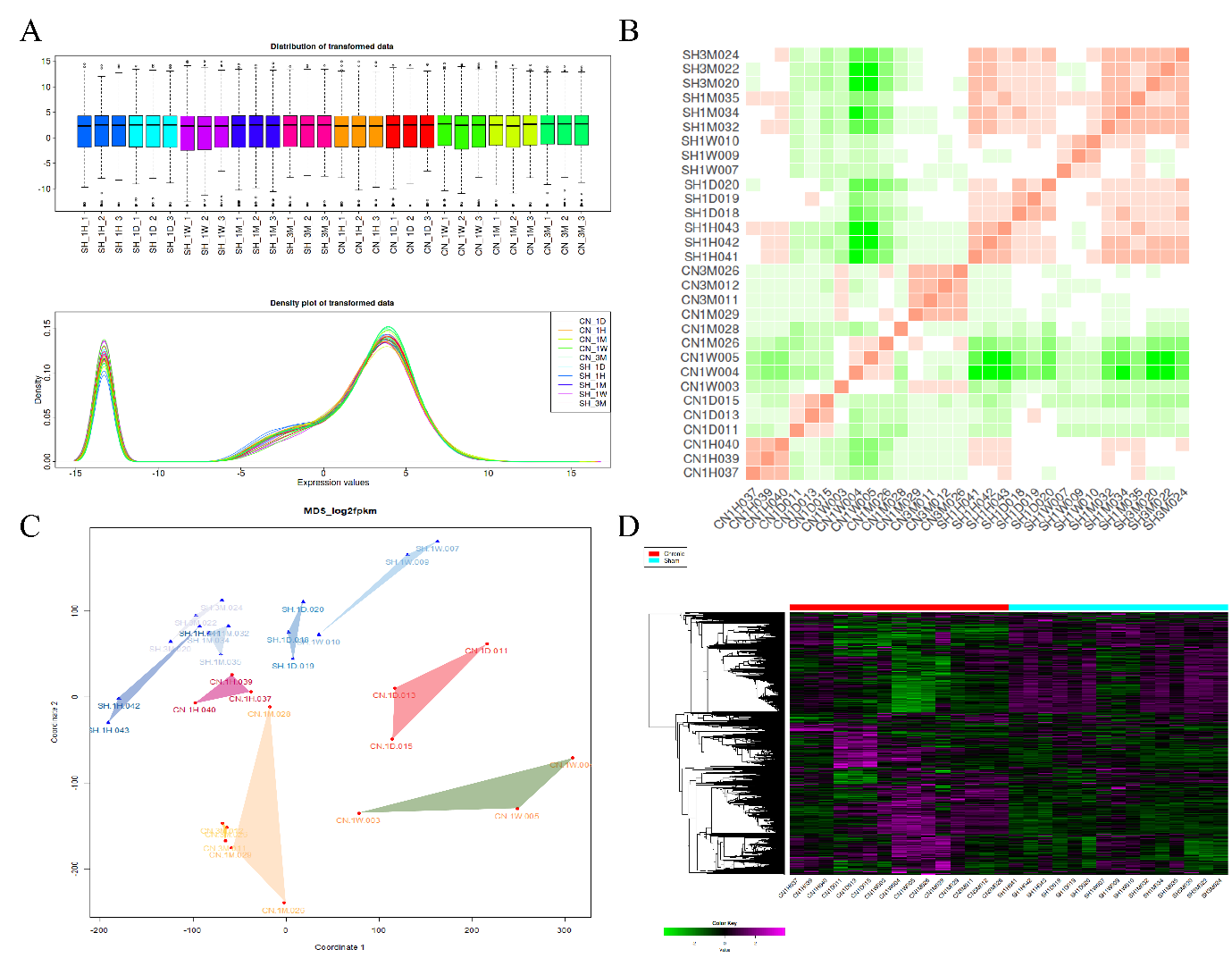
**Table S6. Significantly enriched Reactome pathway with 2,841 DEGs, separated by each time period**

Data available at <https://www.dropbox.com/s/upiikbs1tqrccpl/Supplementary%20Table%20S6_Reactome.xlsx?dl=0>

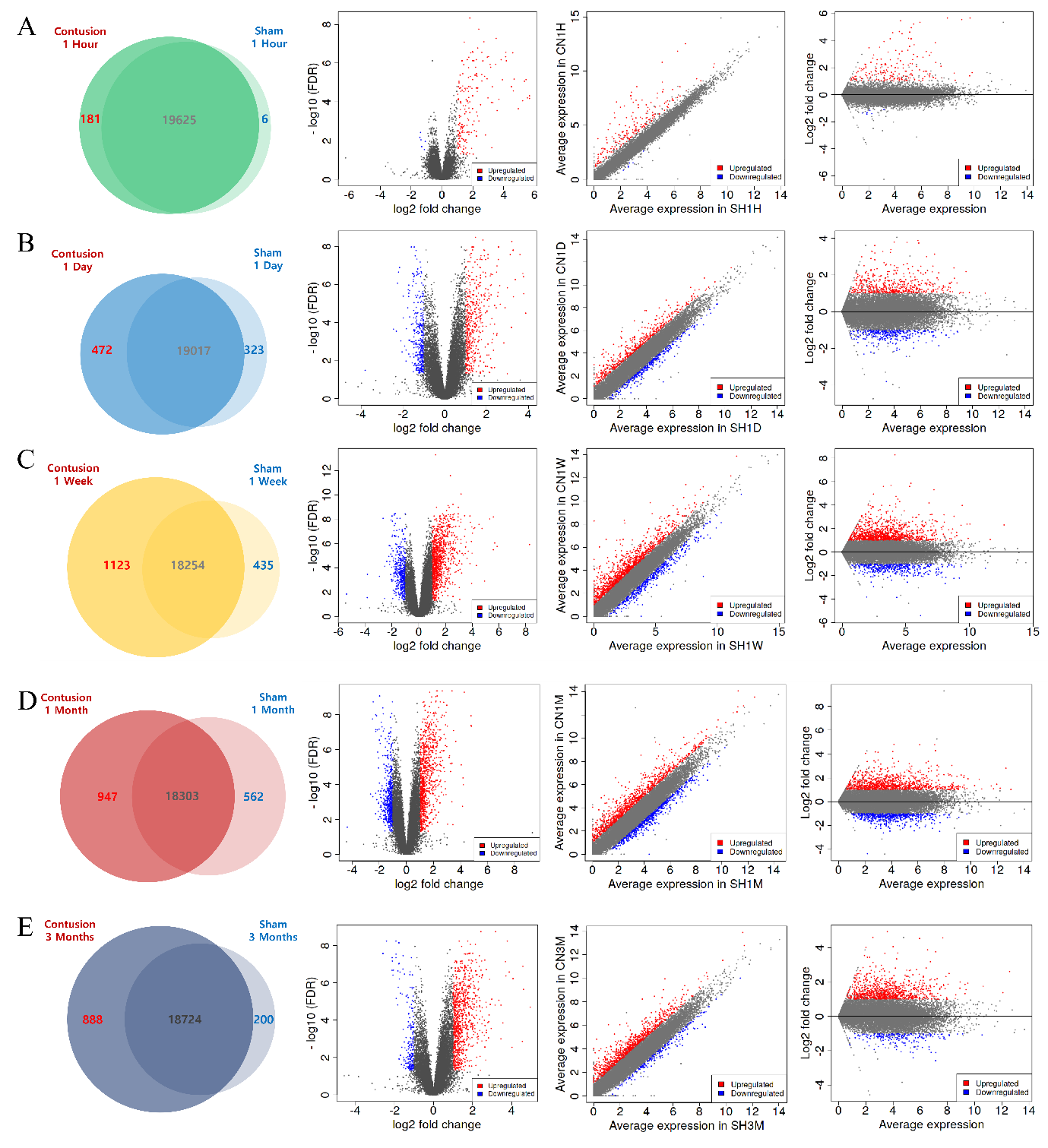
**Table S7. Detailed information for gene-drug interactions**

Data available at <https://www.dropbox.com/s/geflcrim3li7psi/Supplementary%20Table%20S7_Raw-Gene-Drug%20interaction.xlsx?dl=0>

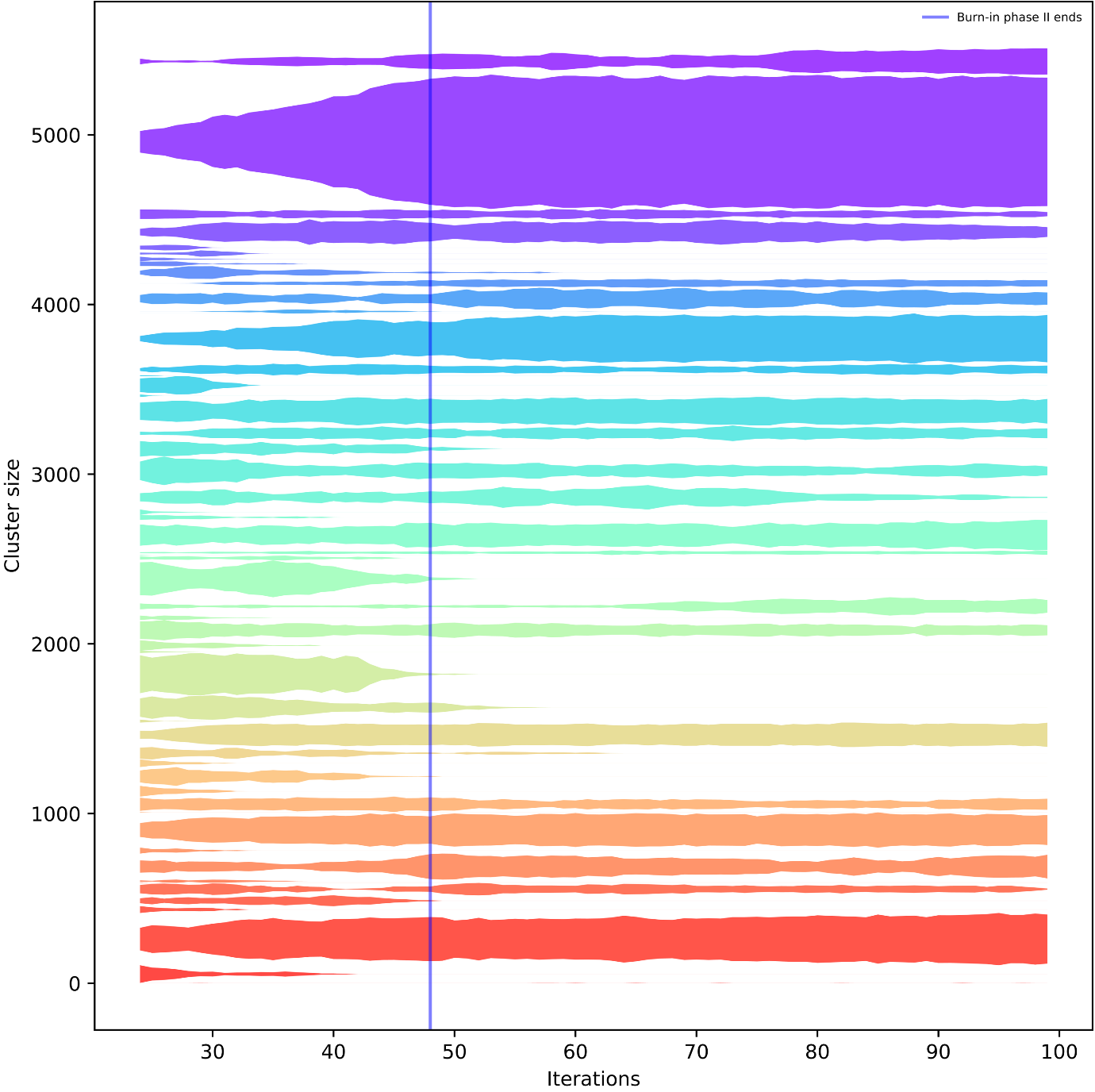
**Supplemental figures**

****

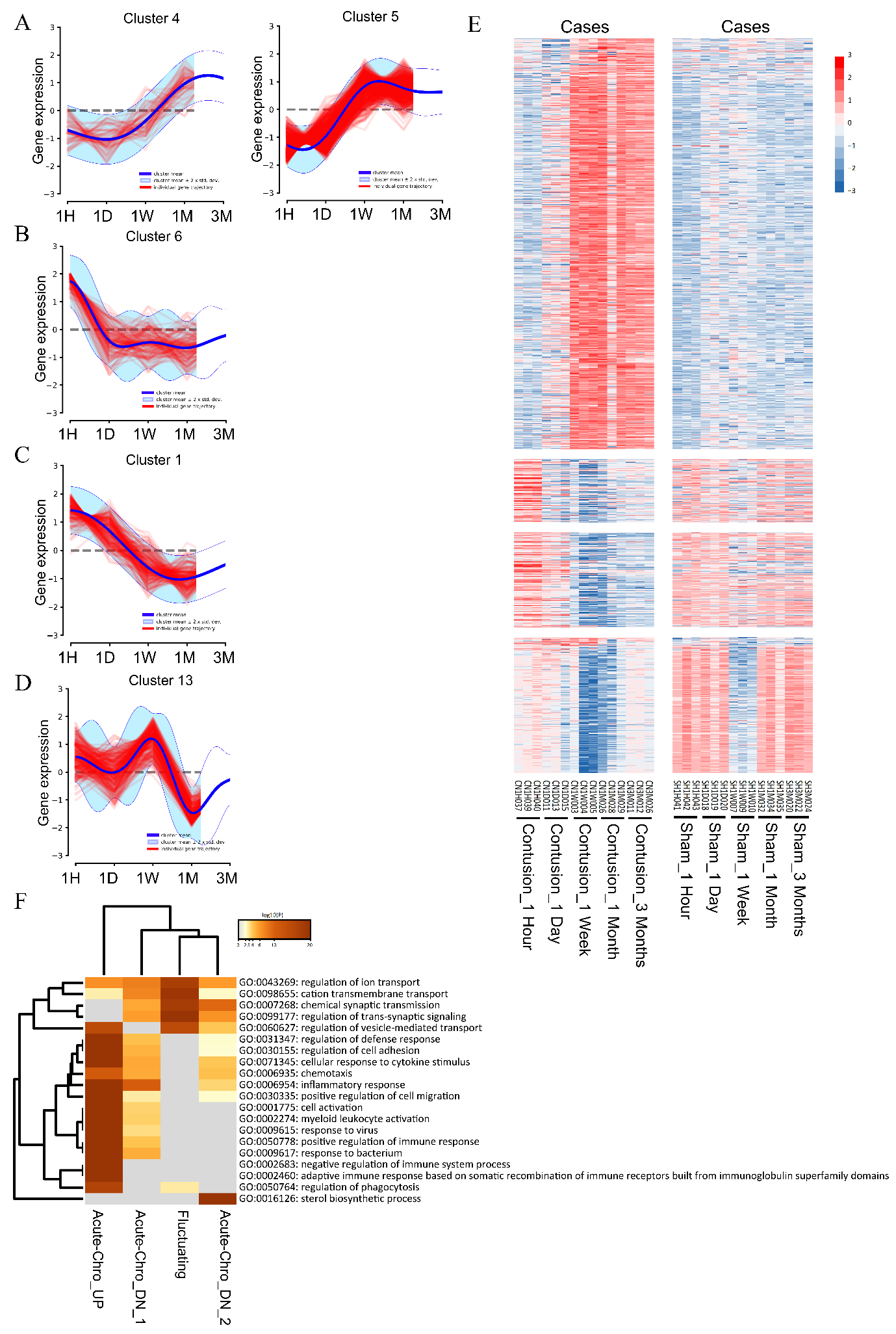
**Figure S1. Bioinformatical observation of expression data and sample correlation.** (A) The boxplot shows the gene expression of each sample subsequent to data normalization. The ordinate represents the gene expression value, and the abscissa represents the sham and the contusion administration groups with independent colors. The distribution of FPKM values for total expressed genes in samples from each group is also shown. (B) The Euclidean distances based on all raw expression data were calculated between each sample, and the colors indicate the distances. The red mosaic color indicates that the gene expression between samples is similar. (C) The MDS plot shows how similar and close the transcriptome changes of each sample are based on the global gene expression level. (D) Hierarchical clustering analysis of total expressed genes is shown. A histogram in the bottom color key shows the number of expression values.

****

**Figure S2. Statistical comparison of DEGs identified at 5 time points.** The number of up- and downregulated genes identified in the 5 comparison sets are separately shown by 5 time points: (A) one hour, (B) one day, (C) one week, (D) one month, and (E) 3 months. Overlapping areas in the Venn diagram represent the genes that do not change with time. The size of the circle is proportional to the number of DEGs in each comparison set. The FPKM volcano, scatter, and MA plots were constructed by pairwise comparison between the contusion and sham groups during the same period. In this statistical analysis, red and blue dots represent the statistically significant up- and downregulated DEGs. The middle line in black dots indicates no difference in the mean expression values between samples.

****

**Figure S3. Iterations analysis to determine the appropriate cluster size and the determined clustering ratio results of 22 clusters. A** heatmap displays the proportion of DPGP samples from the Markov chain in which each gene (on the rows and columns) clusters with every other gene in the time series and shows the posterior similarity matrix obtained from clustering. Ward's linkage clustered rows and columns.



**Figure S4.** (A)Clustered trajectories of genes selected into ‘Acute-Chro\_UP’ (upregulation pattern from 1 hour to 3 months, A), ‘Acute-Chro\_DN\_1’ (downregulation pattern from 1 hour to 3 months, B), ‘Acute-Chro\_DN\_2’ (downregulation pattern from 1 day to 3 months, C), ‘Fluctuating’ (no defined pattern), and D), for the extra module representing the long term. For each cluster, standardized log2-fold change waves (red line) in expression from 5 periods are shown for individual gene trajectories, and the sky-blue boundaries indicate the posterior cluster mean and ±2 standard deviations according to the cluster-specific GP. (E) The heatmap results with actual expression levels of each module isolated from the extra module representing the long term. (F) The functional classification for the related genes within each module are screened and visualized.

****

**Figure S5. The detailed expression pattern of each Reactome pathway.** Volcanic changes in the expression of (A) interleukin signaling, (B) neutrophil degranulation, (C) eukaryotic translation, and (D) collagen degradation-associated gene sets are represented by red dots. The genes related to (E) LGI-ADAM interactions, (F) GABA receptor, and (G) L1CAM- ankyrin interactions pathways are represented by the blue dots.