## Supplemental Figure legends

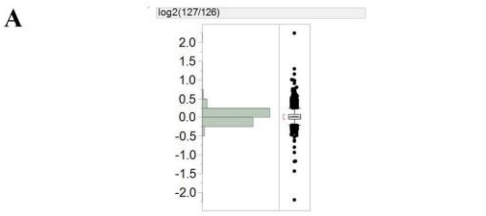
**Supplementary Fig. 1** The ratio distribution and DEP cutoff settings. The ratio distribution of 4697 proteins in the CCI/naïve (A) and AAV-gPTEN/AAV-gNull (B) groups. According to two side 0.95 Prediction interval, the DEP cutoff was calculated and shown (>0.38 or <-0.18 for CCI/Control; >0.30 or <-0.25 for AAV-gPTEN/AAV-gNull).

**Supplementary Fig. 2** CCI induces glial activation in the spinal dorsal horn. (A-F) Immunofluorescence staining of GFAP (A, C, and E) and CD11b/c (B, D, and F) in the spinal dorsal horn in rats at 7 days of sham, 7 days of CCI, and 14 days of CCI. Scale bar, 200 μm. (G and H) Immunofluorescence intensity analysis showing that the immunoreactivity of GFAP (G) and CD11b/c (H) in the ipsilateral spinal dorsal horn was increased at postoperative days 7 and 14 in the CCI group compared with the sham group. n = 3 rats/group. ** $p < 0.01$ compared with the ipsilateral dorsal horn in the sham group, ## $p < 0.01$ compared with the contralateral dorsal horn in the same group, two-way ANOVA followed by post hoc Bonferroni's test. (I-L) Immunofluorescence staining and analysis of NeuN in the spinal dorsal horn in rats at 7 days of sham, 7 days of CCI, and 14 days of CCI. Scale bar, 200 μm. n = 3 rats/group. ** $p < 0.01$ compared with the ipsilateral dorsal horn in the sham group.

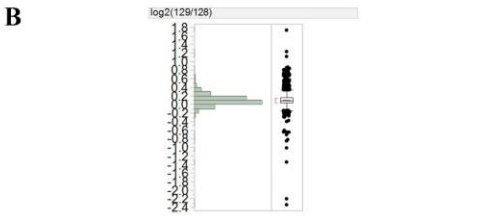
**Supplementary Fig. 3** Astrocytic PTEN and cholesterol alleviates central sensitization and inhibits neuronal activity. (A) Representative western blots and quantification of TNF-α, IL-1β, and IL-6 after i.t. injection of AAV-gPTEN. n = 3. (B) Representative western bolts and quantification of TNF-α, IL-1β, and IL-6 after i.t. injection of AAV-gHMGCR. n= 3. (C) Examples of c-Fos expression in the ipsilateral dorsal horn in naïve rats at sham 21 days, CCI 21 days and i.t. injection AAV (AAV-gPTEN or AAV-gNull) at CCI 21 days. Scale bar, 100 μm. (D) Quantification of c-Fos-expressing neurons in the spinal dorsal horn. n = 3 rats per group. (E) Representative western blots and quantification of c-Fos. n = 3. (F) Examples and quantification of c-Fos expression in the ipsilateral dorsal horn after i.t. injection cholesterol rats at CCI 14 days. Scale bar, 100 μm. n= 3. *compared with Sham group; #compared with AAV-gNull group. *or #$p < 0.05$; **or ##$p < 0.01$; ***or ###$p < 0.001$.

**Supplementary Fig. 4** Identification of PTEN conditional knockout mice. (A-D) Immunostaining shows that PTEN was expressed in NeuN-positive neurons but not in CD11b/c-positive microglia in both littermate and PTEN conditional knockout (Pten CKO) mice. Scale bar, 50 μm. (E) Photographs of littermate and Pten CKO mice show no changes in the gross anatomy of Pten CKO mice. (F and G) Pten CKO mice show normal innervations of CGRP (F) and IB4 (G). CGRP+ peptidergic and IB4 nonpeptidergic primary afferents were well separated in littermate and Pten CKO mice. Scale bar, 100 μm.

## Supplementary Fig. 1

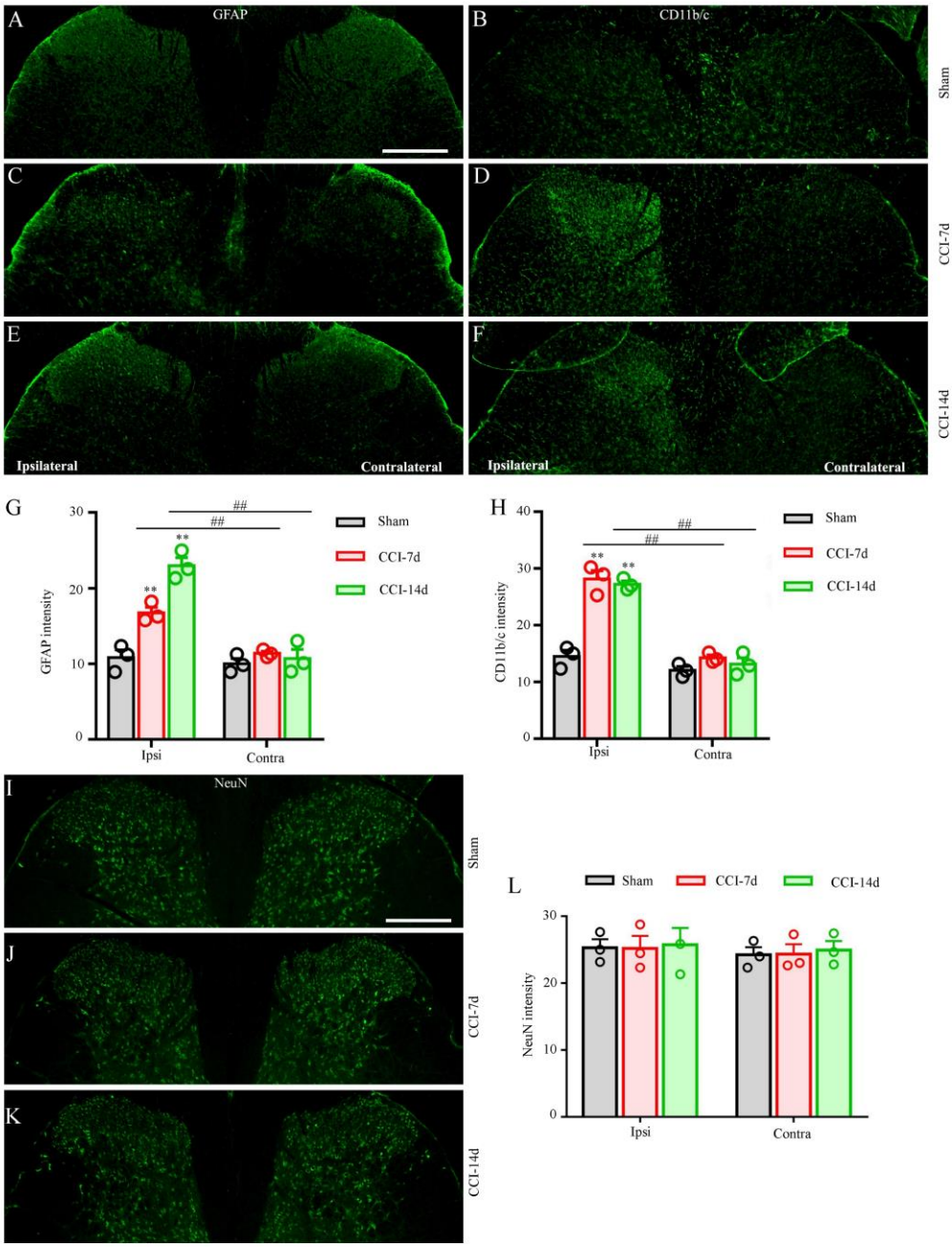



| Prediction Interval | | | | |
|---|---|---|---|---|
| Parameter | Future N | Lower PI | Upper PI | 1-Alpha |
| Individual | 1 | -0.1772 | 0.383117 | 0.950 |
| Mean | 1 | -0.1772 | 0.383117 | 0.950 |
| Std Dev | 1 | . | . | 0.950 |

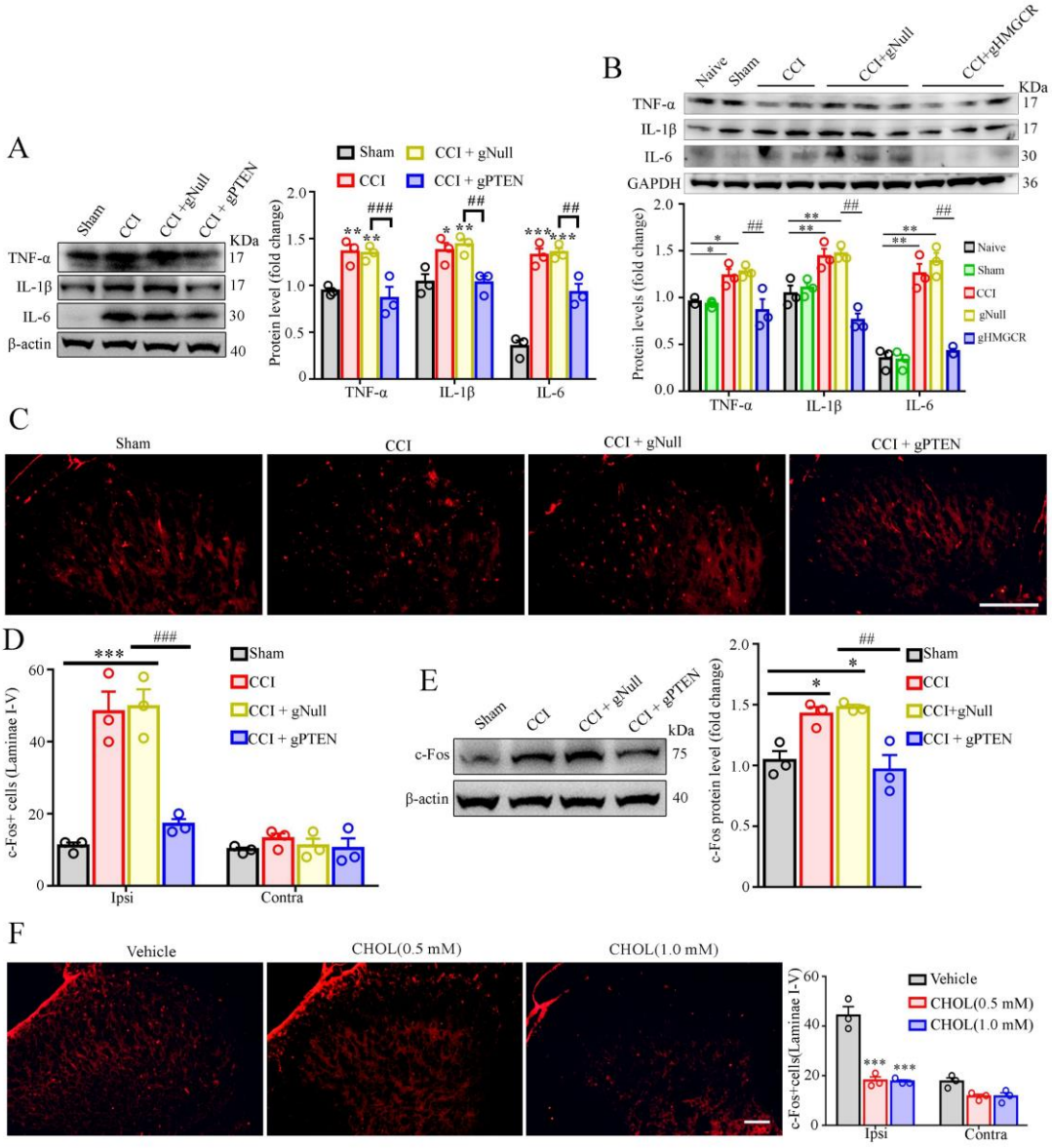



| Prediction Interval | | | | |
|---|---|---|---|---|
| Parameter | Future N | Lower PI | Upper PI | 1-Alpha |
| Individual | 1 | -0.25073 | 0.297974 | 0.950 |
| Mean | 1 | -0.25073 | 0.297974 | 0.950 |
| Std Dev | 1 | . | . | 0.950 |

## Supplementary Fig. 2



**Supplementary Fig. 3**



**Supplementary Fig. 4**

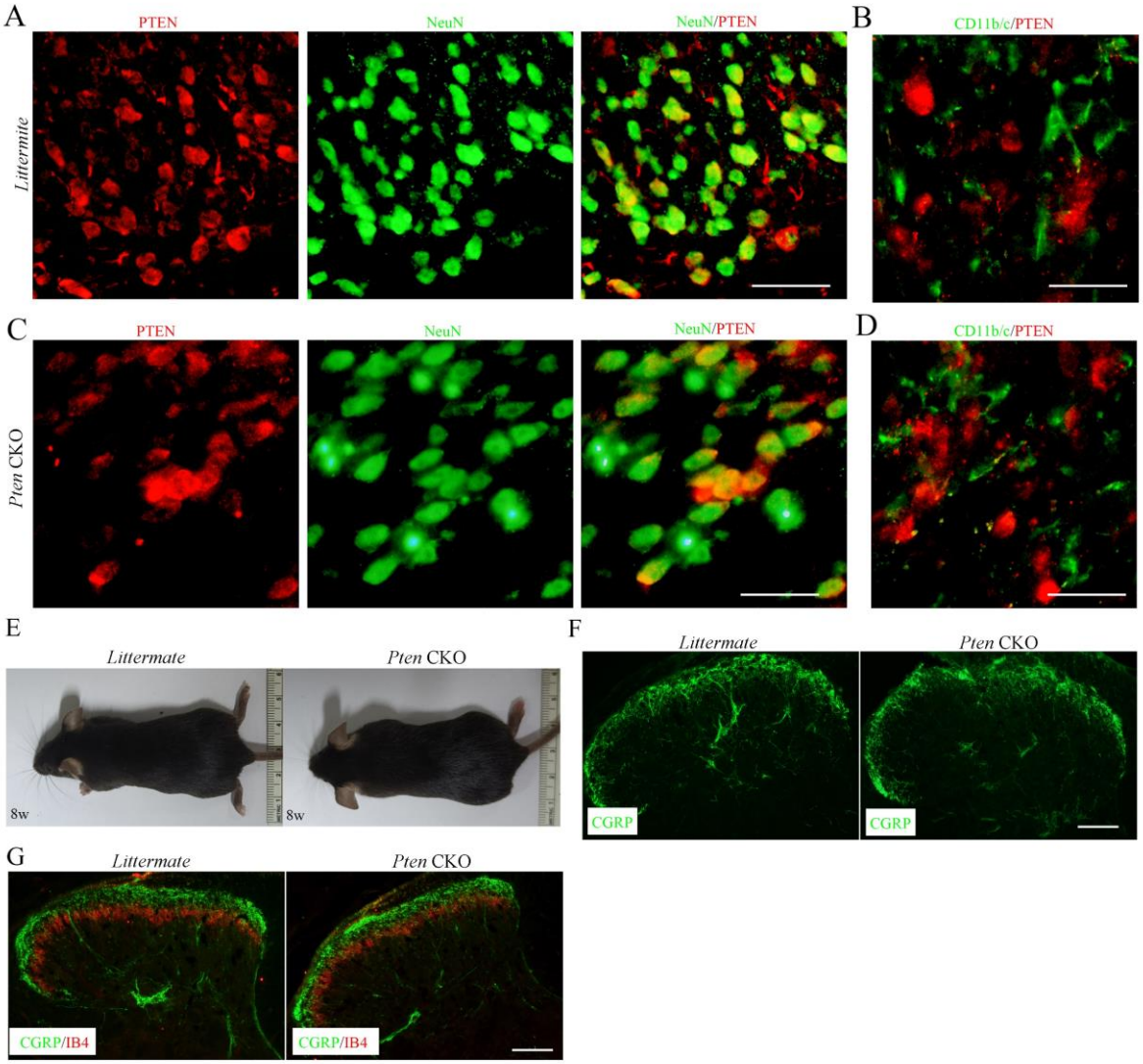


**Table S1. The DEPs cluster**

| Accession | Abundance Ratio: (F1, 127) / (F1, 126) | Abundance Ratio: (F1, 129) / (F1, 128) 2 | log2(127/126) | log2(129/128) | Sum PEP Score | Coverage | # Peptides |
|---|---|---|---|---|---|---|---|
| A0A0G2K139 | 0.92 | 1.21 | 0.30 | 0.28 | 13.41 | 2.83 | 3 |
| Q9Z2N6 | 0.92 | 1.37 | 0.30 | 0.45 | 15.27 | 35.44 | 2 |
| F1LUR9 | 0.92 | 1.42 | 0.30 | 0.51 | 6.52 | 2.90 | 1 |
| B2GV08 | 0.93 | 1.29 | 0.30 | 0.36 | 5.90 | 15.92 | 2 |
| G3V8A4 | 0.93 | 1.31 | 0.30 | 0.38 | 5.17 | 1.84 | 2 |
| D3ZCV0 | 0.93 | 1.34 | 0.30 | 0.43 | 47.68 | 12.42 | 9 |
| Q4KLP0 | 0.93 | 1.46 | 0.30 | 0.54 | 2.90 | 1.96 | 1 |
| M0R5A9 | 0.93 | 1.27 | 0.31 | 0.34 | 7.52 | 4.09 | 3 |
| M0RAY7 | 0.93 | 1.25 | 0.31 | 0.32 | 3.56 | 1.45 | 1 |
| Q5I0L7 | 0.93 | 1.59 | 0.31 | 0.67 | 4.65 | 5.71 | 1 |
| P28077 | 0.93 | 1.36 | 0.31 | 0.45 | 6.41 | 4.11 | 1 |
| D3ZDW3 | 0.93 | 1.23 | 0.31 | 0.30 | 15.59 | 5.34 | 4 |
| B0BMZ1 | 0.93 | 1.29 | 0.31 | 0.37 | 17.77 | 26.67 | 2 |
| F1LR60 | 0.93 | 1.36 | 0.31 | 0.45 | 8.24 | 4.52 | 3 |
| G3V663 | 0.94 | 1.25 | 0.32 | 0.32 | 6.24 | 4.02 | 2 |
| A0A0G2JUZ0 | 0.94 | 1.28 | 0.32 | 0.36 | 4.48 | 2.38 | 1 |
| A0A0G2JZ48 | 0.94 | 1.41 | 0.32 | 0.50 | 8.17 | 3.66 | 3 |
| Q6YDN7 | 0.94 | 1.27 | 0.32 | 0.35 | 4.68 | 38.82 | 2 |
| D3ZU83 | 0.94 | 1.46 | 0.33 | 0.55 | 6.35 | 3.92 | 1 |
| F1LMU0 | 0.94 | 1.33 | 0.33 | 0.41 | 7.31 | 1.55 | 3 |
| A0A0G2JYZ1 | 0.95 | 1.23 | 0.33 | 0.30 | 3.85 | 1.21 | 1 |
| D3ZVH6 | 0.95 | 1.29 | 0.34 | 0.37 | 6.11 | 2.85 | 1 |
| D3ZTL2 | 0.95 | 1.49 | 0.35 | 0.57 | 5.06 | 2.92 | 2 |
| F1LNL3 | 0.96 | 1.34 | 0.36 | 0.42 | 5.14 | 1.19 | 2 |
| A0A096MJT6 | 0.96 | 1.36 | 0.36 | 0.44 | 3.32 | 0.34 | 1 |
| B2RYB8 | 0.96 | 1.21 | 0.36 | 0.28 | 13.30 | 8.59 | 5 |
| P20761 | 0.97 | 1.20 | 0.36 | 0.27 | 10.82 | 7.81 | 2 |
| Q6AXS8 | 0.97 | 1.75 | 0.37 | 0.80 | 3.29 | 5.41 | 1 |
| Q5PQW8 | 0.97 | 1.31 | 0.37 | 0.39 | 10.13 | 3.21 | 2 |
| Q9Z1W6 | 0.97 | 1.23 | 0.37 | 0.29 | 29.89 | 17.38 | 8 |
| P53676 | 0.98 | 1.38 | 0.38 | 0.47 | 30.63 | 19.62 | 6 |
| A0A0G2K7W4 | 0.98 | 1.30 | 0.38 | 0.38 | 8.10 | 1.78 | 2 |
| Q9JJK4 | 0.98 | 1.75 | 0.39 | 0.80 | 3.93 | 4.84 | 1 |
| Q4V797 | 0.98 | 1.68 | 0.39 | 0.75 | 3.08 | 4.56 | 1 |
| A0A140TAJ0 | 0.99 | 1.62 | 0.39 | 0.70 | 10.48 | 6.87 | 3 |
| Q920D2 | 0.99 | 1.24 | 0.40 | 0.31 | 7.40 | 5.35 | 1 |
| D3ZSZ0 | 0.99 | 1.28 | 0.40 | 0.36 | 2.77 | 6.09 | 1 |
| B2RYT4 | 1.00 | 1.28 | 0.41 | 0.35 | 4.07 | 11.72 | 1 |
| Q02769 | 1.00 | 1.28 | 0.41 | 0.35 | 7.69 | 5.77 | 2 |
| D3ZPP9 | 1.00 | 1.23 | 0.41 | 0.29 | 2.96 | 6.40 | 1 |
| B2GV05 | 1.01 | 1.21 | 0.42 | 0.27 | 7.24 | 3.19 | 2 |
| Q68FS9 | 1.03 | 1.75 | 0.46 | 0.81 | 3.75 | 12.87 | 2 |
| Q63538 | 1.04 | 1.32 | 0.46 | 0.40 | 6.98 | 10.35 | 3 |
| A0A0G2JSP8 | 1.05 | 1.42 | 0.48 | 0.51 | 27.53 | 22.83 | 7 |
| Q5XJW2 | 1.05 | 1.24 | 0.48 | 0.31 | 4.10 | 7.02 | 1 |
| D4A5W8 | 1.05 | 1.27 | 0.48 | 0.34 | 5.01 | 3.14 | 1 |
| F1M4G6 | 1.05 | 1.79 | 0.49 | 0.84 | 20.96 | 17.24 | 5 |
| D4A5A6 | 1.08 | 1.28 | 0.52 | 0.35 | 4.16 | 0.91 | 1 |
| Q63433 | 1.08 | 1.40 | 0.52 | 0.49 | 4.64 | 2.96 | 2 |
| Q497C3 | 1.11 | 1.49 | 0.56 | 0.58 | 4.87 | 7.35 | 1 |
| Q6MGB5 | 1.11 | 1.27 | 0.56 | 0.35 | 11.75 | 14.67 | 2 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| G3V8L6 | 1.12 | 1.27 | 0.57 | 0.34 | 3.85 | 2.08 | 1 |
| Q6AYT0 | 1.13 | 1.43 | 0.59 | 0.51 | 18.87 | 12.16 | 3 |
| Q6AY69 | 1.14 | 1.60 | 0.60 | 0.68 | 3.31 | 5.05 | 1 |
| D4A9N5 | 1.15 | 1.42 | 0.62 | 0.50 | 5.20 | 2.95 | 2 |
| D4A7F0 | 1.16 | 1.24 | 0.63 | 0.31 | 7.03 | 1.53 | 3 |
| Q62760 | 1.21 | 1.26 | 0.69 | 0.34 | 3.28 | 13.10 | 2 |
| Q7TP54 | 1.21 | 1.35 | 0.69 | 0.43 | 3.51 | 0.99 | 1 |
| D3ZCT5 | 1.22 | 1.37 | 0.70 | 0.45 | 3.75 | 2.10 | 2 |
| M0R439 | 1.23 | 1.35 | 0.71 | 0.43 | 10.11 | 6.86 | 3 |
| D3ZAQ4 | 1.26 | 1.66 | 0.75 | 0.73 | 4.81 | 9.47 | 2 |
| D3ZGY1 | 1.27 | 1.36 | 0.76 | 0.45 | 4.19 | 5.42 | 1 |
| P55009 | 1.31 | 1.22 | 0.80 | 0.29 | 15.31 | 23.13 | 3 |
| P02600 | 1.40 | 1.70 | 0.90 | 0.76 | 6.25 | 10.05 | 2 |
| D3ZQE8 | 1.47 | 1.32 | 0.97 | 0.40 | 9.62 | 3.24 | 3 |
| G3V7I7 | 1.49 | 1.09 | 0.99 | 0.13 | 19.30 | 14.12 | 6 |
| D3ZQB6 | 1.50 | 3.32 | 1.00 | 1.73 | 3.54 | 3.10 | 1 |
| B2RZ56 | 1.66 | 2.35 | 1.15 | 1.23 | 3.28 | 6.11 | 1 |
| M0R7S5 | 0.92 | 0.92 | 0.30 | -0.12 | 20.71 | 38.14 | 5 |
| D4A9Q9 | 0.92 | 1.00 | 0.30 | 0.00 | 4.25 | 2.98 | 1 |
| A0A0G2JT62 | 0.93 | 0.87 | 0.30 | -0.20 | 15.23 | 3.36 | 4 |
| A0A0G2K4U7 | 0.93 | 1.18 | 0.30 | 0.24 | 12.73 | 4.15 | 4 |
| A0A0G2K5C6 | 0.93 | 0.85 | 0.30 | -0.24 | 642.02 | 40.81 | 101 |
| D3ZP60 | 0.93 | 1.06 | 0.30 | 0.08 | 5.68 | 2.38 | 2 |
| D4A542 | 0.93 | 1.19 | 0.30 | 0.24 | 4.38 | 3.35 | 2 |
| P70473 | 0.93 | 1.04 | 0.31 | 0.06 | 9.80 | 10.73 | 4 |
| Q4KM31 | 0.93 | 1.06 | 0.31 | 0.08 | 5.48 | 11.72 | 2 |
| D3ZYS7 | 0.93 | 1.18 | 0.31 | 0.23 | 10.15 | 8.82 | 3 |
| G3V7V0 | 0.93 | 1.05 | 0.31 | 0.07 | 5.23 | 2.69 | 2 |
| Q9R141 | 0.93 | 1.13 | 0.31 | 0.18 | 3.80 | 1.99 | 1 |
| D3ZTG3 | 0.93 | 1.15 | 0.31 | 0.21 | 3.28 | 1.71 | 1 |
| Q68FT9 | 0.93 | 1.16 | 0.31 | 0.21 | 6.47 | 6.25 | 2 |
| P11348 | 0.94 | 1.06 | 0.32 | 0.08 | 133.92 | 59.75 | 10 |
| Q3B7U1 | 0.94 | 1.15 | 0.32 | 0.21 | 6.91 | 2.75 | 2 |
| G3V8V8 | 0.94 | 1.07 | 0.32 | 0.09 | 5.58 | 3.56 | 2 |
| A0A0G2K8Z9 | 0.94 | 1.10 | 0.32 | 0.13 | 7.49 | 1.30 | 2 |
| M0R715 | 0.94 | 1.13 | 0.32 | 0.17 | 16.43 | 3.18 | 3 |
| Q9JMC1 | 0.94 | 1.05 | 0.32 | 0.07 | 5.53 | 2.10 | 2 |
| P23928 | 0.94 | 1.05 | 0.32 | 0.07 | 15.24 | 12.00 | 2 |
| Q62636 | 0.94 | 1.11 | 0.32 | 0.14 | 37.02 | 38.04 | 6 |
| B2RYP8 | 0.94 | 1.04 | 0.33 | 0.06 | 4.19 | 1.66 | 2 |
| D3ZBP4 | 0.94 | 1.15 | 0.33 | 0.21 | 7.82 | 2.01 | 2 |
| Q923M1 | 0.94 | 1.07 | 0.33 | 0.10 | 12.11 | 18.03 | 3 |
| A0A0G2JW12 | 0.94 | 1.11 | 0.33 | 0.15 | 38.24 | 4.26 | 6 |
| Q02765 | 0.94 | 1.14 | 0.33 | 0.19 | 10.63 | 7.27 | 2 |
| Q5XIC2 | 0.95 | 1.04 | 0.33 | 0.06 | 9.78 | 4.84 | 2 |
| A0A0G2K0T5 | 0.95 | 1.10 | 0.33 | 0.13 | 5.30 | 4.16 | 2 |
| Q01750 | 0.95 | 1.16 | 0.33 | 0.22 | 5.63 | 6.02 | 2 |
| Q8VIL3 | 0.95 | 0.96 | 0.33 | -0.06 | 26.08 | 24.81 | 6 |
| F1LPW0 | 0.95 | 1.09 | 0.33 | 0.13 | 8.80 | 4.65 | 2 |
| G3V913 | 0.95 | 1.18 | 0.33 | 0.24 | 58.61 | 49.03 | 9 |
| D3ZU55 | 0.95 | 0.97 | 0.34 | -0.04 | 3.11 | 2.76 | 2 |
| P27881 | 0.95 | 1.08 | 0.34 | 0.10 | 29.00 | 7.20 | 6 |
| Q2KN99 | 0.95 | 1.16 | 0.35 | 0.22 | 11.85 | 2.06 | 2 |
| Q6P9U0 | 0.96 | 1.09 | 0.35 | 0.12 | 37.47 | 19.26 | 7 |
| F1MAQ7 | 0.96 | 1.10 | 0.35 | 0.14 | 11.40 | 1.55 | 3 |
| P52944 | 0.96 | 1.14 | 0.35 | 0.19 | 9.65 | 11.31 | 3 |
| P58775 | 0.96 | 1.03 | 0.36 | 0.04 | 64.97 | 25.35 | 10 |
| D4A8G5 | 0.96 | 1.07 | 0.36 | 0.09 | 3.42 | 2.48 | 2 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| G3V6L0 | 0.96 | 0.89 | 0.36 | -0.17 | 4.62 | 6.67 | 1 |
| Q568Y8 | 0.96 | 1.11 | 0.36 | 0.15 | 6.95 | 8.87 | 3 |
| D4A3X0 | 0.97 | 0.96 | 0.37 | -0.07 | 9.17 | 0.80 | 3 |
| D4AAV4 | 0.97 | 1.08 | 0.37 | 0.11 | 8.96 | 4.70 | 3 |
| F1LR67 | 0.97 | 1.02 | 0.37 | 0.03 | 7.01 | 1.38 | 2 |
| Q4AEF8 | 0.97 | 1.15 | 0.37 | 0.20 | 33.94 | 17.16 | 10 |
| Q6YH22 | 0.97 | 1.12 | 0.37 | 0.17 | 6.03 | 21.05 | 1 |
| Q68FR2 | 0.97 | 1.08 | 0.37 | 0.11 | 17.75 | 11.05 | 5 |
| B5DEJ9 | 0.97 | 1.15 | 0.38 | 0.20 | 10.37 | 3.12 | 4 |
| D4AED6 | 0.98 | 1.11 | 0.39 | 0.15 | 3.31 | 3.56 | 1 |
| D3ZVU4 | 0.99 | 1.10 | 0.39 | 0.14 | 4.02 | 6.81 | 2 |
| O55232 | 0.99 | 1.05 | 0.40 | 0.07 | 3.82 | 10.00 | 1 |
| D3ZA85 | 0.99 | 1.06 | 0.40 | 0.08 | 10.87 | 14.23 | 3 |
| F1M6Q3 | 0.99 | 1.17 | 0.40 | 0.23 | 11.22 | 1.64 | 2 |
| G3V6W2 | 1.00 | 1.12 | 0.41 | 0.16 | 16.31 | 6.71 | 2 |
| P20767 | 1.01 | 0.93 | 0.43 | -0.10 | 10.18 | 40.38 | 3 |
| Q3MHU5 | 1.02 | 1.12 | 0.44 | 0.16 | 3.13 | 2.03 | 1 |
| D3ZD80 | 1.03 | 1.12 | 0.45 | 0.16 | 5.82 | 2.81 | 2 |
| B0BN19 | 1.03 | 1.04 | 0.46 | 0.05 | 13.29 | 19.59 | 3 |
| Q66HA4 | 1.03 | 1.11 | 0.46 | 0.15 | 6.34 | 2.95 | 2 |
| D3ZDZ1 | 1.03 | 1.16 | 0.46 | 0.21 | 4.25 | 1.36 | 1 |
| M0R7B4 | 1.04 | 1.01 | 0.47 | 0.01 | 61.78 | 30.00 | 10 |
| D4A1J3 | 1.04 | 1.19 | 0.48 | 0.25 | 39.92 | 18.42 | 9 |
| Q32PX2 | 1.05 | 0.92 | 0.48 | -0.12 | 13.12 | 16.56 | 4 |
| P31720 | 1.05 | 1.19 | 0.48 | 0.24 | 4.86 | 8.16 | 1 |
| Q4V896 | 1.05 | 1.05 | 0.49 | 0.07 | 13.05 | 13.31 | 3 |
| P14669 | 1.07 | 1.15 | 0.52 | 0.20 | 59.29 | 40.43 | 12 |
| A0A0G2JUF9 | 1.08 | 0.94 | 0.52 | -0.08 | 6.23 | 1.50 | 2 |
| A0A140TA91 | 1.10 | 1.06 | 0.55 | 0.08 | 5.02 | 9.87 | 2 |
| A0A0G2K5V4 | 1.10 | 1.16 | 0.55 | 0.21 | 5.82 | 0.92 | 2 |
| Q91Y94 | 1.11 | 1.22 | 0.56 | 0.28 | 3.46 | 6.40 | 1 |
| D3ZYJ5 | 1.12 | 1.19 | 0.57 | 0.24 | 7.57 | 1.25 | 1 |
| Q9WTQ1 | 1.12 | 1.07 | 0.58 | 0.09 | 3.32 | 1.63 | 1 |
| Q5XIC6 | 1.14 | 1.20 | 0.61 | 0.26 | 26.70 | 16.01 | 6 |
| Q6AY80 | 1.83 | 0.82 | 1.29 | -0.29 | 32.65 | 26.84 | 5 |
| D4A9Z2 | 3.55 | 1.10 | 2.24 | 0.13 | 4.21 | 3.94 | 2 |
| F8WGA3 | 0.28 | 1.64 | -1.44 | 0.71 | 38.27 | 19.05 | 7 |
| D4A261 | 0.33 | 1.22 | -1.18 | 0.29 | 4.90 | 1.24 | 1 |
| Q6AYC4 | 0.33 | 1.62 | -1.17 | 0.69 | 6.87 | 9.74 | 2 |
| P80299 | 0.39 | 1.23 | -0.94 | 0.30 | 5.77 | 5.23 | 3 |
| Q4G075 | 0.43 | 1.45 | -0.80 | 0.53 | 49.06 | 22.96 | 9 |
| A0A0G2JSW3 | 0.48 | 1.13 | -0.64 | 0.18 | 139.56 | 77.55 | 11 |
| P54900 | 0.49 | 1.58 | -0.62 | 0.66 | 7.87 | 20.93 | 2 |
| Q5U2U4 | 0.52 | 1.28 | -0.53 | 0.36 | 3.48 | 6.08 | 1 |
| Q5XIE8 | 0.54 | 1.22 | -0.49 | 0.28 | 9.27 | 10.53 | 2 |
| A0A0G2KB18 | 0.54 | 1.18 | -0.47 | 0.24 | 3.42 | 2.01 | 1 |
| B2GV65 | 0.55 | 1.18 | -0.46 | 0.24 | 5.66 | 17.92 | 1 |
| Q9JMI1 | 0.55 | 1.11 | -0.46 | 0.15 | 16.14 | 5.80 | 4 |
| A0A0G2K5Y1 | 0.55 | 1.30 | -0.46 | 0.38 | 3.30 | 3.05 | 1 |
| P17256 | 0.55 | 1.24 | -0.44 | 0.31 | 35.27 | 21.52 | 5 |
| D4AAI7 | 0.55 | 1.12 | -0.44 | 0.16 | 5.86 | 11.90 | 2 |
| A0A0G2K2Q2 | 0.56 | 1.51 | -0.42 | 0.59 | 6.97 | 10.10 | 2 |
| A0A0G2JYA2 | 0.57 | 0.64 | -0.41 | -0.65 | 14.15 | 9.12 | 3 |
| Q923V8 | 0.57 | 1.13 | -0.41 | 0.17 | 5.96 | 9.88 | 1 |
| A0A0G2K329 | 0.57 | 1.16 | -0.40 | 0.21 | 53.50 | 12.00 | 10 |
| P12007 | 0.57 | 0.96 | -0.40 | -0.05 | 89.71 | 35.38 | 14 |
| P38062 | 0.58 | 1.21 | -0.38 | 0.27 | 26.69 | 11.51 | 4 |
| A0A0G2JXT3 | 0.58 | 1.06 | -0.38 | 0.08 | 56.56 | 23.10 | 10 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| H1UBN0 | 0.58 | 1.16 | -0.38 | 0.22 | 5.76 | 4.68 | 2 |
| Q3B8N9 | 0.58 | 1.12 | -0.37 | 0.16 | 13.79 | 13.06 | 3 |
| D3ZN38 | 0.58 | 1.26 | -0.36 | 0.33 | 6.26 | 9.39 | 2 |
| P17425 | 0.59 | 1.15 | -0.35 | 0.20 | 82.49 | 26.92 | 14 |
| Q66HG6 | 0.59 | 1.66 | -0.35 | 0.73 | 5.85 | 5.36 | 1 |
| O35093 | 0.59 | 1.28 | -0.35 | 0.36 | 7.73 | 8.13 | 1 |
| Q63666 | 0.59 | 1.30 | -0.34 | 0.38 | 37.23 | 33.90 | 3 |
| O88407 | 0.60 | 1.18 | -0.33 | 0.24 | 13.22 | 7.28 | 2 |
| F1LU27 | 0.60 | 1.27 | -0.33 | 0.35 | 5.13 | 1.45 | 2 |
| P38718 | 0.60 | 0.96 | -0.33 | -0.06 | 6.61 | 8.66 | 1 |
| B2RZB7 | 0.60 | 1.19 | -0.33 | 0.25 | 3.62 | 16.81 | 1 |
| D4AD89 | 0.60 | 1.06 | -0.33 | 0.08 | 6.48 | 3.53 | 2 |
| D3ZCF8 | 0.60 | 1.14 | -0.33 | 0.19 | 19.10 | 4.31 | 5 |
| D3ZZ62 | 0.60 | 1.17 | -0.33 | 0.23 | 4.15 | 2.20 | 1 |
| Q4KLL0 | 0.60 | 1.20 | -0.32 | 0.27 | 8.81 | 11.96 | 3 |
| P51639 | 0.61 | 1.12 | -0.31 | 0.16 | 3.08 | 0.90 | 1 |
| Q498T9 | 0.61 | 1.21 | -0.31 | 0.27 | 3.83 | 2.24 | 1 |
| Q9QYW3 | 0.61 | 1.17 | -0.31 | 0.23 | 11.55 | 12.44 | 2 |
| G3V8W2 | 0.61 | 1.18 | -0.31 | 0.24 | 38.75 | 17.12 | 6 |
| P63041 | 0.61 | 1.06 | -0.30 | 0.09 | 75.11 | 57.46 | 6 |
| P06302 | 0.61 | 1.19 | -0.30 | 0.25 | 22.40 | 13.39 | 4 |
| A0A0G2K658 | 0.61 | 1.13 | -0.30 | 0.18 | 78.50 | 39.51 | 10 |
| P69735 | 0.61 | 1.16 | -0.30 | 0.21 | 41.87 | 14.84 | 9 |
| G3V7M5 | 0.62 | 1.19 | -0.29 | 0.25 | 7.93 | 6.78 | 2 |
| Q05175 | 0.62 | 1.30 | -0.29 | 0.38 | 156.70 | 83.64 | 17 |
| F1M8A4 | 0.62 | 1.11 | -0.28 | 0.15 | 26.47 | 6.87 | 6 |
| Q5FVL3 | 0.62 | 1.17 | -0.28 | 0.23 | 3.91 | 3.71 | 1 |
| Q4G073 | 0.62 | 1.49 | -0.28 | 0.58 | 3.53 | 4.09 | 1 |
| D3ZX08 | 0.62 | 1.23 | -0.28 | 0.29 | 3.75 | 1.22 | 1 |
| G3V8U8 | 0.62 | 0.95 | -0.28 | -0.08 | 12.60 | 10.69 | 3 |
| F1LM42 | 0.62 | 0.84 | -0.28 | -0.25 | 455.33 | 26.57 | 85 |
| A0A0H2UHM2 | 0.62 | 1.08 | -0.28 | 0.10 | 3.42 | 2.95 | 1 |
| G3V7J7 | 0.62 | 0.95 | -0.27 | -0.08 | 26.82 | 32.68 | 4 |
| P03889 | 0.62 | 1.09 | -0.27 | 0.13 | 6.33 | 6.29 | 2 |
| D4ADS4 | 0.62 | 1.15 | -0.27 | 0.20 | 3.26 | 9.21 | 1 |
| Q6AY55 | 0.62 | 1.22 | -0.27 | 0.28 | 6.24 | 5.42 | 2 |
| P97888 | 0.62 | 1.21 | -0.27 | 0.27 | 7.98 | 6.71 | 3 |
| Q62967 | 0.62 | 1.18 | -0.27 | 0.24 | 51.69 | 17.71 | 5 |
| A0JN25 | 0.62 | 0.95 | -0.27 | -0.08 | 97.68 | 51.31 | 16 |
| M0R809 | 0.62 | 1.19 | -0.27 | 0.25 | 19.34 | 64.00 | 3 |
| D4A4H5 | 0.63 | 1.02 | -0.26 | 0.02 | 4.12 | 6.39 | 1 |
| G3V790 | 0.63 | 1.21 | -0.26 | 0.28 | 7.78 | 2.42 | 3 |
| P69897 | 0.63 | 1.08 | -0.26 | 0.10 | 308.90 | 72.97 | 25 |
| A0A0G2K1L4 | 0.63 | 1.13 | -0.26 | 0.17 | 6.21 | 2.79 | 1 |
| A0A0U1RRU5 | 0.63 | 1.13 | -0.26 | 0.18 | 2.79 | 2.59 | 1 |
| D3ZDX7 | 0.63 | 1.14 | -0.26 | 0.19 | 9.15 | 9.95 | 2 |
| A0A0G2KAX2 | 0.63 | 0.83 | -0.26 | -0.27 | 7.15 | 4.31 | 2 |
| Q4FZU0 | 0.63 | 1.15 | -0.26 | 0.21 | 7.94 | 7.51 | 3 |
| D4AAV5 | 0.63 | 1.16 | -0.26 | 0.21 | 4.03 | 3.82 | 1 |
| D4AD70 | 0.63 | 1.04 | -0.25 | 0.06 | 21.51 | 50.00 | 5 |
| F1M4H5 | 0.63 | 1.25 | -0.25 | 0.32 | 22.91 | 15.68 | 5 |
| M0R9L3 | 0.63 | 1.00 | -0.25 | 0.00 | 5.45 | 2.36 | 1 |
| G3V6R0 | 0.16 | 0.20 | -2.20 | -2.34 | 63.27 | 25.94 | 8 |
| P06907 | 0.95 | 0.22 | 0.34 | -2.20 | 15.54 | 12.90 | 3 |

**Table S2. The GO terms**

| Category | Term | Count | % | PValue | Genes |
|---|---|---|---|---|---|
| GOTERM_BP_DIRECT | GO:0008299~isoprenoid biosynthetic process | 5.00 | 6.76 | 0.00 | A0A0G2JXT3, P17256, P17425, Q62967, P51639 |
| GOTERM_BP_DIRECT | GO:0006695~cholesterol biosynthetic process | 5.00 | 6.76 | 0.00 | A0A0G2JXT3, P17256, P17425, Q62967, P51639 |
| GOTERM_BP_DIRECT | GO:0006886~intracellular protein transport | 7.00 | 9.46 | 0.00 | A0A0G2JYA2, O35093, M0R9L3, A0A0G2K5Y1, Q63666, Q5U2U4, D3ZZ62 |
| GOTERM_BP_DIRECT | GO:0006551~leucine metabolic process | 2.00 | 2.70 | 0.01 | P12007, G3V8U8 |
| GOTERM_BP_DIRECT | GO:0019287~isopentenyl diphosphate biosynthetic process, mevalonate pathway | 2.00 | 2.70 | 0.01 | P17256, Q62967 |
| GOTERM_BP_DIRECT | GO:0014074~response to purine-containing compound | 2.00 | 2.70 | 0.02 | P17425, Q9JMI1 |
| GOTERM_BP_DIRECT | GO:0010243~response to organonitrogen compound | 3.00 | 4.05 | 0.03 | P17425, D4ADS4, Q9JMI1 |
| GOTERM_BP_DIRECT | GO:0007399~nervous system development | 4.00 | 5.41 | 0.04 | G3V790, P54900, F1LM42, Q5XIE8 |
| GOTERM_BP_DIRECT | GO:0070723~response to cholesterol | 2.00 | 2.70 | 0.05 | A0A0G2JXT3, P17425 |
| GOTERM_BP_DIRECT | GO:0021680~cerebellar Purkinje cell layer development | 2.00 | 2.70 | 0.05 | O88407, D4AD89 |
| GOTERM_BP_DIRECT | GO:0071397~cellular response to cholesterol | 2.00 | 2.70 | 0.06 | P17425, Q9JMI1 |

| | | | | | |
|---|---|---|---|---|---|
| GOTERM_BP_DIRECT | GO:0009058~biosynthetic process | 2.00 | 2.70 | 0.07 | A0A0G2K2Q2, G3V7M5 |
| GOTERM_BP_DIRECT | GO:0007584~response to nutrient | 3.00 | 4.05 | 0.09 | A0JN25, P51639, Q9JMI1 |
| GOTERM_BP_DIRECT | GO:0035904~aorta development | 2.00 | 2.70 | 0.10 | G3V790, A0A0U1RRU5 |
| GOTERM_BP_DIRECT | GO:0086091~regulation of heart rate by cardiac conduction | 2.00 | 2.70 | 0.10 | P54900, F1LM42 |