

**Supplementary Materials:**
**Table S1. Summary of primers used for qPCR analysis. F : forward primer, R : reverse primer.**

| Gene           |   | Sequence (5' to 3')      |
|----------------|---|--------------------------|
| <i>ACTB</i>    | F | GATCAAGATCATTGCTCCTCCTGA |
|                | R | ACGCAGCTCAGTAACAGTCC     |
| <i>ADH5</i>    | F | CGAACCAGGTGATCAGGTGTAA   |
|                | R | GTATAGGCATCGGTGTGGCA     |
| <i>ADORA2B</i> | F | GCTTCTGCACGGACTTTTAC     |
|                | R | AACCTTTATACCTGAGCGGGAC   |
| <i>ATG10</i>   | F | GGCAAGCTTTTTAGATGGGAGAC  |
|                | R | GTTGCCCAAGTATTGGATGCTC   |
| <i>BAX</i>     | F | ACACCTGAGCTGACCTTGGA     |
|                | R | AGTTCATCGCCAATTCGCCT     |
| <i>BCL2</i>    | F | CTGGTGGACAACATCGCTCT     |
|                | R | TCCACAAAGGCATCCCAGC      |
| <i>BDNF</i>    | F | TACCTGGATGCCGAAACAT      |
|                | R | TGGCCTTTTGATACCGGGAC     |
| <i>BNIP3</i>   | F | AAAACAGCACTCTGTCTGAGGAA  |
|                | R | TTTCTGGCCGACTTGACCAAT    |
| <i>CAPN1</i>   | F | TCATTCCAGCTGTGGCAGT      |
|                | R | AGCTTCCATCCTTGGTGGG      |
| <i>CAPN2</i>   | F | GAGGCATTGCCGAGTGGTAT     |
|                | R | GACGGAGTACGCATGTCCTT     |
| <i>CAST</i>    | F | TGGCACTGAGAGGAGAGACA     |
|                | R | TGGATCAGGCTGTCTTTGTCC    |
| <i>CASP3</i>   | F | GGAGCTTGGAACGCGAAGA      |
|                | R | TACACAAGCCCATTTCAGGGT    |
| <i>CAT</i>     | F | CCGCCTTTTGCTTACCCAG      |
|                | R | GAGCACGGTAGGGACAGTTC     |
| <i>CCNA2</i>   | F | AGTGCCGCTGTCTCTTACC      |
|                | R | GGGGTGATTCAAACTACCATCC   |
| <i>CRB1</i>    | F | CGTGTACTTGGCCCTTTGC      |
|                | R | TCAGGATAGAAGGGGTGGGG     |
| <i>CDK1</i>    | F | GAACAGAGAGGGTCCGTTGTAA   |
|                | R | GTA CTGGGCACTCCTTCTTCC   |
| <i>CDK2</i>    | F | CTTTGCCGAAATGGTGACCC     |
|                | R | TAACTCCTGGCCAAACCACC     |
| <i>CYCS</i>    | F | CTTGGGCTAGAGAGCGGGA      |
|                | R | CCCATTTTAAATTCGGTCCGGG   |

|         |   |                         |
|---------|---|-------------------------|
| FOS     | F | CCCTGTCAACACACAGGACTT   |
|         | R | GCTGTCACCGTGGGGATAAA    |
| GJA1    | F | AGGTCTGAGAGCCTGAACTCT   |
|         | R | CTGGGCACCTCTCTTTCACCTA  |
| EGF     | F | AGAACGATGTCAGCACCGAG    |
|         | R | CTGCTTCCGAGTCTGTAGTAG   |
| MAPK3   | F | AACCCAAACAAGCGCATCAC    |
|         | R | AGCCACTGGTTCATCTGTCC    |
| MAPK1   | F | CTTAAATTGGTCAGGACAAGGGC |
|         | R | CGGCTCAAAGGAGTCAAGAGT   |
| FZD4    | F | CACCACTGTCCAACCTCCTC    |
|         | R | TCTACCCTACACAGGGCTCC    |
| GABARAP | F | CTGTACCAGGAACACCATGAAGA |
|         | R | GCGCCACCTCTCTTTGTAGA    |
| GAPDH   | F | AGTGCCAGCCTCGTCTCATA    |
|         | R | GGTAACCAGGCGTCCGATAC    |
| GCL     | F | TGTCGCTGGGGAGTGATTTC    |
|         | R | GATTGTCTTCAGGGGCTCCA    |
| GDNF    | F | CACCAGATAAACAAGCGGGCG   |
|         | R | TCGTAGCCCAAACCCAAGTC    |
| GFAP    | F | AACGTTAAGCTAGCCCTGGAC   |
|         | R | CAGGAATGGTGATGCGGTTTT   |
| GFRA1   | F | CCAGCCAGAGTCAAGGTCTG    |
|         | R | TGACTGTGCCAATCAGTCCC    |
| GPX1    | F | GGTAGGTCCAGACGGTGTTTC   |
|         | R | ATCGGGTTCGATGTCGATGG    |
| GSS     | F | TGTGCACCGACATGTTCTCA    |
|         | R | CTCGTTCTCTATGGCACGCT    |
| IL1R1   | F | CCAAGACCTACGGAGAGGGA    |
|         | R | ACCTCGATGGTATCTTCCCA    |
| IL6     | F | GAGTGGCTAAGGACCAAGACC   |
|         | R | TAGCACACTAGGTTGCCGAG    |
| MAPK8   | F | TGCTGGTGATAGATGCGTCC    |
|         | R | CCAGACGTTGATGTACGGGT    |
| LC3B    | F | AAGAGTGGAAGATGTCCGGC    |
|         | R | TGCAGGCGCCTTCTAATTATCT  |
| LPA1    | F | CCGACTCACGAGTTGCTTCT    |
|         | R | CTGTGAACTGGGGCTGTGAA    |
| MAPK14  | F | CCAGCTTCAGCAGATAATGCG   |
|         | R | TGTAGTTTCTGCCTCATGGCT   |

|        |   |                            |
|--------|---|----------------------------|
| CCL2   | F | CTGTAGCATCCACGTGCTGT       |
|        | R | AGTTCTCCAGCCGACTCATTG      |
| MTOR   | F | CACCCATCCAACCTGATGCT       |
|        | R | ATCGAGACCGGTAACCTCCA       |
| MYD88  | F | CCTGTCTCCAGGTGTCCAAC       |
|        | R | GGGTCCAGAACCAGGACTTG       |
| NFKB1  | F | TGCAACAGATGGCCCATACC       |
|        | R | TTGCAGGCCCCACATAGTT        |
| NGF    | F | CATCGCTCTCCTTCACAGAGTT     |
|        | R | GACATTACGCTATGCACCTCAG     |
| NGFR   | F | GCTGCTGCTGATTCTAGGGAT      |
|        | R | GAGAATGTAACACTGTCCAGGCA    |
| NFE2L2 | F | CATTTGTAGATGACCATGAGTCGC   |
|        | R | CGTATTAAGACACTGTAACCTCGGGA |
| P2Y4   | F | TAAGGAAGCTAGGGGGCCAT       |
|        | R | CGGAAGAGGAACAGCCAGAG       |
| PRKACA | F | ATCTATCAGAGAAAGGTGGAAGCTC  |
|        | R | ACAAGCACACCCCTAAAACCTCA    |
| RAGE   | F | TGAGGTAGGGCATGAGGATGA      |
|        | R | ATCACCGGTTTCTGTGACCCT      |
| REDD1  | F | GCTAGCTGCGGCTTCTGT         |
|        | R | GGAGGACGAGAAACGATCCC       |
| RELA   | F | GATAACCGTGCCCCCAACA        |
|        | R | AGCCAGGTCCCGTGAAATAC       |
| RHOA   | F | CGGGAAGCAGGTAGAGTTGG       |
|        | R | TGTCTGGGTAGGAGAGAGGC       |
| S100B  | F | TTCCTGGAGGAAATCAAAGAGCA    |
|        | R | GAAGTCACACTCCCCATCCC       |
| SOD1   | F | TGGGGACAATACACAAGGCTG      |
|        | R | TCCAACATGCCTCTCTTCATCC     |
| SOD2   | F | GCCTCAGCAATGTTGTGTCG       |
|        | R | ATTGTTACGTAGGTCGCGT        |
| SOX10  | F | CAAGCTCTGGAGGTTGCTGA       |
|        | R | GGGCTGCCTTCCCATTCTT        |
| TGFB1  | F | GCTGAACCAAGGAGACGGAATA     |
|        | R | CCTCGACGTTTGGGACTGAT       |
| TLR4   | F | ACTGGGTGAGAAACGAGCTG       |
|        | R | CAGCAATGGCTACACCAGGA       |
| TRPV1  | F | AGGGAGATCCATGAACCCGA       |
|        | R | CATGTCATGACGGTTAGGGGT      |

|     |   |                       |
|-----|---|-----------------------|
| VIM | F | GCTGCGAGAAAAATTGCAGGA |
|     | R | GGTCAAGACGTGCCAGAGAA  |

**Table S2. Relative gene expression in EGCs after 24 hrs exposure to PTX2, YTX and AZA1.** The gene expression was carried out by RT-qPCR. Values are normalized to the reference gene GAPDH and presented as mean  $\pm$  SEM. Three independent experiments were performed.

| Biological function | Gene   |      | Control | PTX2  | PTX2  | PTX2  | YTX   | YTX   | YTX  | AZA1    | AZA1    | AZA1   |
|---------------------|--------|------|---------|-------|-------|-------|-------|-------|------|---------|---------|--------|
|                     |        |      |         | 1 nM  | 2 nM  | 4 nM  | 1 nM  | 2 nM  | 4 nM | 0.38 nM | 0.75 nM | 1.5 nM |
| Viability           | ATG10  | Mean | 5.85    | 7.41  | 6.07  | 4.76  | 6.76  | 5.04  | 6.56 | 6.80    | 7.19    | 6.65   |
|                     |        | SEM  | 0.73    | 1.24  | 0.56  | 0.54  | 0.49  | 0.88  | 0.52 | 0.55    | 0.32    | 1.64   |
|                     | BAX    | Mean | 0.96    | 1.04  | 1.07  | 0.84  | 0.95  | 1.04  | 0.91 | 1.00    | 1.07    | 1.00   |
|                     |        | SEM  | 0.12    | 0.10  | 0.01  | 0.03  | 0.02  | 0.06  | 0.02 | 0.03    | 0.12    | 0.07   |
|                     | CAPN1  | Mean | 0.83    | 0.99  | 0.96  | 0.83  | 0.89  | 0.81  | 0.81 | 0.90    | 0.71    | 0.77   |
|                     |        | SEM  | 0.08    | 0.05  | 0.11  | 0.07  | 0.08  | 0.13  | 0.06 | 0.04    | 0.11    | 0.05   |
|                     | CAPN2  | Mean | 0.96    | 1.20  | 1.16  | 1.06  | 1.09  | 1.10  | 0.99 | 1.09    | 1.10    | 1.21   |
|                     |        | SEM  | 0.03    | 0.08  | 0.15  | 0.06  | 0.04  | 0.05  | 0.09 | 0.05    | 0.09    | 0.05   |
|                     | LC3B   | Mean | 1.07    | 1.07  | 1.12  | 0.82  | 1.03  | 1.02  | 1.09 | 1.00    | 1.19    | 1.22   |
|                     |        | SEM  | 0.07    | 0.16  | 0.24  | 0.21  | 0.06  | 0.10  | 0.17 | 0.15    | 0.04    | 0.04   |
|                     | MTOR   | Mean | 4.80    | 5.58  | 5.25  | 4.06  | 4.73  | 4.55  | 4.27 | 5.24    | 4.44    | 4.66   |
|                     |        | SEM  | 0.50    | 0.64  | 0.22  | 0.49  | 0.13  | 0.48  | 0.05 | 0.46    | 0.25    | 0.14   |
| REDD1               | Mean   | 3.94 | 4.31    | 4.60  | 3.03  | 4.59  | 4.56  | 4.32  | 4.32 | 4.42    | 4.45    |        |
|                     | SEM    | 0.36 | 0.31    | 0.53  | 0.50  | 0.28  | 0.26  | 0.27  | 0.38 | 0.37    | 0.29    |        |
| Inflammation        | IL6    | Mean | 13.26   | 12.57 | 18.70 | 65.14 | 13.09 | 20.21 | 3.35 | 11.32   | 15.89   | 14.75  |
|                     |        | SEM  | 2.74    | 1.90  | 5.58  | 44.25 | 4.85  | 10.58 | 0.48 | 3.44    | 10.62   | 5.37   |
|                     | MAPK1  | Mean | 3.43    | 4.11  | 4.28  | 3.61  | 3.49  | 3.29  | 3.21 | 3.85    | 3.32    | 3.51   |
|                     |        | SEM  | 0.53    | 0.16  | 0.26  | 0.24  | 0.44  | 0.24  | 0.28 | 0.73    | 0.51    | 0.51   |
|                     | MAPK3  | Mean | 1.05    | 1.11  | 1.14  | 0.86  | 1.17  | 0.96  | 0.96 | 1.12    | 1.16    | 1.07   |
|                     |        | SEM  | 0.03    | 0.05  | 0.11  | 0.09  | 0.03  | 0.06  | 0.03 | 0.02    | 0.05    | 0.07   |
|                     | MAPK8  | Mean | 0.57    | 0.80  | 0.82  | 0.74  | 0.77  | 0.66  | 0.77 | 0.83    | 0.75    | 0.78   |
|                     |        | SEM  | 0.08    | 0.07  | 0.08  | 0.04  | 0.03  | 0.05  | 0.03 | 0.03    | 0.04    | 0.09   |
|                     | MAPK14 | Mean | 4.16    | 5.10  | 4.87  | 3.76  | 4.69  | 3.83  | 4.07 | 5.70    | 4.97    | 5.00   |

|                  |       |       |       |       |       |       |       |       |       |       |       |      |
|------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|
|                  |       | SEM   | 0.38  | 0.82  | 0.23  | 0.37  | 0.20  | 0.42  | 0.20  | 0.94  | 0.83  | 0.11 |
|                  | MCP1  | Mean  | 0.49  | 0.69  | 0.53  | 0.46  | 0.70  | 1.07  | 0.90  | 0.87  | 1.14  | 1.22 |
|                  |       | SEM   | 0.19  | 0.04  | 0.01  | 0.08  | 0.05  | 0.15  | 0.12  | 0.19  | 0.01  | 0.14 |
|                  | NFKB1 | Mean  | 4.15  | 4.60  | 5.27  | 5.01  | 5.27  | 3.37  | 3.85  | 4.16  | 4.23  | 2.98 |
|                  |       | SEM   | 0.89  | 0.25  | 0.44  | 0.30  | 0.75  | 0.60  | 0.22  | 0.18  | 1.11  | 0.09 |
|                  | RELA  | Mean  | 1.07  | 1.05  | 1.05  | 0.92  | 0.94  | 0.99  | 1.05  | 0.69  | 1.04  | 1.03 |
|                  |       | SEM   | 0.02  | 0.02  | 0.14  | 0.13  | 0.05  | 0.08  | 0.15  | 0.04  | 0.08  | 0.08 |
| Oxidative stress | ADH5  | Mean  | 5.08  | 5.50  | 5.91  | 3.91  | 5.14  | 4.51  | 4.88  | 5.57  | 5.14  | 5.50 |
|                  |       | SEM   | 0.08  | 0.52  | 0.06  | 0.68  | 0.31  | 0.14  | 0.10  | 0.29  | 0.20  | 0.24 |
|                  | CAST  | Mean  | 1.03  | 1.18  | 1.11  | 1.10  | 1.04  | 1.11  | 0.98  | 1.14  | 1.12  | 1.15 |
|                  |       | SEM   | 0.06  | 0.06  | 0.07  | 0.11  | 0.03  | 0.11  | 0.04  | 0.06  | 0.03  | 0.07 |
|                  | CRB1  | Mean  | 3.38  | 4.11  | 3.59  | 3.77  | 3.94  | 4.44  | 3.52  | 4.91  | 4.03  | 5.06 |
|                  |       | SEM   | 0.21  | 0.41  | 0.11  | 0.48  | 0.17  | 0.24  | 0.16  | 1.11  | 0.07  | 0.50 |
|                  | CYCS  | Mean  | 1.10  | 1.23  | 1.17  | 1.04  | 1.06  | 0.99  | 0.98  | 1.24  | 1.19  | 1.20 |
|                  |       | SEM   | 0.03  | 0.03  | 0.01  | 0.07  | 0.03  | 0.04  | 0.05  | 0.09  | 0.05  | 0.05 |
|                  | GCL   | Mean  | 0.70  | 0.60  | 0.96  | 0.85  | 0.69  | 0.82  | 0.82  | 0.95  | 0.85  | 1.00 |
|                  |       | SEM   | 0.07  | 0.08  | 0.07  | 0.10  | 0.09  | 0.11  | 0.08  | 0.18  | 0.02  | 0.09 |
|                  | GPX1  | Mean  | 1.07  | 1.10  | 1.23  | 1.05  | 1.05  | 0.77  | 0.73  | 0.94  | 0.90  | 0.90 |
|                  |       | SEM   | 0.12  | 0.09  | 0.22  | 0.07  | 0.15  | 0.11  | 0.12  | 0.31  | 0.11  | 0.02 |
|                  | GSS   | Mean  | 3.88  | 5.24  | 3.71  | 2.92  | 4.56  | 3.69  | 4.16  | 4.44  | 4.24  | 3.09 |
|                  |       | SEM   | 0.39  | 0.71  | 0.09  | 0.53  | 0.49  | 0.65  | 0.31  | 0.30  | 0.63  | 0.21 |
|                  | SOD1  | Mean  | 0.91  | 1.06  | 0.92  | 0.86  | 0.95  | 0.94  | 0.91  | 0.95  | 1.01  | 1.07 |
|                  |       | SEM   | 0.04  | 0.10  | 0.08  | 0.05  | 0.02  | 0.07  | 0.01  | 0.03  | 0.02  | 0.10 |
| SOD2             | Mean  | 10.81 | 11.81 | 11.04 | 11.20 | 10.56 | 12.22 | 13.72 | 11.14 | 11.46 | 14.24 |      |
|                  | SEM   | 1.02  | 1.05  | 1.10  | 2.08  | 0.92  | 1.07  | 0.74  | 1.13  | 1.48  | 1.74  |      |

|                      |         |      |       |       |       |       |       |        |       |        |       |       |
|----------------------|---------|------|-------|-------|-------|-------|-------|--------|-------|--------|-------|-------|
| Gliomediator         | EGF     | Mean | 6.45  | 4.91  | 6.54  | 5.01  | 5.06  | 5.33   | 3.42  | 5.87   | 4.77  | 5.41  |
|                      |         | SEM  | 0.56  | 0.96  | 1.27  | 0.11  | 0.07  | 1.31   | 0.71  | 1.09   | 0.90  | 0.66  |
|                      | NGF     | Mean | 28.36 | 18.16 | 16.50 | 16.14 | 19.84 | 21.59  | 17.28 | 32.12  | 20.41 | 23.27 |
|                      |         | SEM  | 6.85  | 1.71  | 0.87  | 1.25  | 4.42  | 0.64   | 6.60  | 5.46   | 1.48  | 10.17 |
|                      | S100B   | Mean | 0.82  | 0.96  | 0.91  | 0.75  | 0.90  | 0.97   | 1.01  | 0.96   | 1.05  | 1.11  |
|                      |         | SEM  | 0.02  | 0.14  | 0.16  | 0.02  | 0.08  | 0.07   | 0.05  | 0.01   | 0.04  | 0.12  |
| TGFB1                | Mean    | 0.80 | 0.92  | 0.93  | 1.03  | 0.88  | 0.80  | 0.79   | 0.91  | 0.88   | 0.81  |       |
|                      | SEM     | 0.01 | 0.13  | 0.15  | 0.10  | 0.06  | 0.06  | 0.09   | 0.03  | 0.03   | 0.08  |       |
| Channel and receptor | ADORA2B | Mean | 63.06 | 19.09 | 43.04 | 38.87 | 47.20 | 102.82 | 35.33 | 154.39 | 54.80 | 55.36 |
|                      |         | SEM  | 29.88 | 16.67 | 20.26 | 23.51 | 37.44 | 100.01 | 12.79 | 100.00 | 18.13 | 26.93 |
|                      | P2Y4    | Mean | 18.49 | 15.20 | 15.39 | 21.42 | 17.11 | 13.89  | 15.21 | 17.23  | 16.02 | 13.49 |
|                      |         | SEM  | 2.16  | 4.79  | 4.14  | 4.65  | 0.39  | 1.02   | 1.52  | 2.03   | 1.08  | 3.20  |
|                      | NGFR    | Mean | 0.73  | 0.91  | 0.89  | 0.97  | 0.86  | 0.80   | 0.94  | 0.84   | 1.00  | 0.97  |
|                      |         | SEM  | 0.02  | 0.08  | 0.16  | 0.13  | 0.06  | 0.04   | 0.06  | 0.07   | 0.05  | 0.05  |
|                      | RAGE    | Mean | 14.49 | 9.67  | 17.51 | 14.19 | 12.58 | 10.21  | 10.92 | 12.85  | 13.52 | 10.71 |
|                      |         | SEM  | 2.03  | 2.63  | 2.65  | 2.57  | 1.47  | 2.60   | 1.99  | 1.68   | 2.89  | 3.36  |
| TRPV1                | Mean    | 5.01 | 1.55  | 5.99  | 5.94  | 3.99  | 3.99  | 3.54   | 3.80  | 3.66   | 2.77  |       |
|                      | SEM     | 3.17 | 0.62  | 2.53  | 2.54  | 1.06  | 0.27  | 0.40   | 1.52  | 0.32   | 0.43  |       |
| Morphology           | ACTB    | Mean | 1.13  | 1.18  | 1.06  | 0.86  | 1.07  | 0.88   | 0.72  | 1.16   | 0.95  | 0.88  |
|                      |         | SEM  | 0.01  | 0.02  | 0.01  | 0.05  | 0.02  | 0.03   | 0.00  | 0.16   | 0.13  | 0.04  |
|                      | PRKACA  | Mean | 0.89  | 1.15  | 1.14  | 1.02  | 0.97  | 0.84   | 0.71  | 0.95   | 1.08  | 0.87  |
|                      |         | SEM  | 0.06  | 0.18  | 0.13  | 0.25  | 0.10  | 0.08   | 0.08  | 0.07   | 0.06  | 0.09  |
|                      | SOX10   | Mean | 0.82  | 0.98  | 0.98  | 0.85  | 0.84  | 0.76   | 0.86  | 0.83   | 0.90  | 0.79  |
|                      |         | SEM  | 0.06  | 0.10  | 0.10  | 0.02  | 0.01  | 0.02   | 0.11  | 0.04   | 0.04  | 0.06  |
| VIM                  | Mean    | 0.95 | 1.03  | 1.00  | 0.95  | 0.86  | 0.76  | 0.77   | 0.95  | 0.80   | 0.76  |       |

|  |     |      |      |      |      |      |      |      |      |      |      |
|--|-----|------|------|------|------|------|------|------|------|------|------|
|  | SEM | 0.10 | 0.06 | 0.07 | 0.07 | 0.07 | 0.04 | 0.10 | 0.03 | 0.04 | 0.10 |
|--|-----|------|------|------|------|------|------|------|------|------|------|