

# Supplementary Tables

**Table S1.** List of primer sequences used in RT-qPCR.

| Gene                           | Forward primer (5'-3')    | Reverse primer (5'-3')  |
|--------------------------------|---------------------------|-------------------------|
| <b>Arginase 1</b>              | CTTGGCTTGCTTCGGAAGTC      | GGAGAAGGCGTTTGCTTAGTTC  |
| <b>CX3CL1</b>                  | CTCACGAATCCCAGTGGCTT      | TTTCTCCTTCGGGTCAGCAC    |
| <b>CX3CR1</b>                  | ATGGGGTCTCTGTCTGCTCT      | TACTGGCAATGGGTGGCATT    |
| <b>Cx43</b>                    | ACAGCGGTTGAGTCAGCTTG      | GAGAGATGGGGAAGGACTTGT   |
| <b>Dlg4</b>                    | GAGGCTGGCGGCCAGTACACCAG   | ACAGAGCAGGCGGTCAG       |
| <b>Dynein</b>                  | GCCTCAGTCTCTGTCCCATC      | AAGTCCTGGGGTAAGGTGCT    |
| <b>GFAP</b>                    | CAAAGTGGCTGATGTCTACC      | GCTTCATCTGCCTCCTGTCTA   |
| <b>GPR17</b>                   | AGCTACGAGGAGTCCACCTG      | AGACCGTTTCATCTTGTGGCTCT |
| <b>IL-10</b>                   | ATGCTGCTTGCTCTTACTGA      | GCAGCTCTAGGAGCATGTGG    |
| <b>IL-1<math>\beta</math></b>  | CAGGCTCCGAGATGAACAAC      | GGTGGAGAGCTTTCAGCTCATA  |
| <b>iNOS</b>                    | ACCCACATCTGGCAGAATGAG     | AGCCATGACCTTTCGCATTAG   |
| <b>Kif5b</b>                   | GGTCCTACAGTTGCCACCTA      | ATTGAAATACGCCAGGCCCA    |
| <b>MBP</b>                     | CCATCCAAGAAGACCCACACA     | CCCCTGTCACCGCTAAAGAA    |
| <b>MFG-E8</b>                  | AGCCTGAATGGTAGGGTTGG      | GAGACTGCATCCTGCAACCA    |
| <b>NeuN</b>                    | CCAGGCACTGAGGCCAGCACACAGC | CTCCGTGGGGTCGGAAGGGTGG  |
| <b>P2RY12</b>                  | CACCTCAGCCAATACCACCT      | CAGGACGGTGTACAGCAATG    |
| <b>PLP</b>                     | TGGCGACTACAAGACCACCA      | GACACACCCGCTCCAAAGAA    |
| <b>RPL19</b>                   | ATGAGTATGCTCAGGCTACAGA    | GCATTGGCGATTTTCATTGGTC  |
| <b>S100B</b>                   | GAGAGAGGGTGACAAGCACAA     | GGCCATAAACTCCTGGAAGTC   |
| <b>Synaptophysin</b>           | GACGTTGGTAGTGCCTGTGA      | GCACAGGAAAGTAGGGGGTC    |
| <b>TIMP2</b>                   | AGCCAAAGCAGTGAGCGAGAAG    | GCCGTGTAGATAAACTCGATGTC |
| <b>TMEM119</b>                 | CCCAGAGCTGGTTCCATAGC      | GGGAGTGACACAGAGTAGGC    |
| <b>TNF-<math>\alpha</math></b> | TACTGAACTTCGGGGTGATTGGTCC | CAGCCTTGTCCTTGAAGAGAACC |
| <b>TREM2</b>                   | AACTTCAGATCCTCACTGGACC    | CCTGGCTGGACTTAAGCTGT    |

CX3CL1, C-X3-C motif chemokine ligand 1/fractalkine; CX3CR1, c-x3-c chemokine receptor 1; Cx43, connexin 43; Dlg4, discs large MAGUK scaffold protein 4 (encodes for postsynaptic density protein 95, PSD-95); GFAP, glial fibrillary acidic protein; GPR17, G protein-coupled receptor 17; IL-10, interleukin 10; IL-1 $\beta$ , interleukin 1 $\beta$ ; iNOS, inducible nitric oxide synthase; Kif5b encodes for the protein kinesin -1 heavy chain; MBP, myelin basic protein; MFG-E8, milk fat globule-epidermal growth factor-factor 8; NeuN, hexaribonucleotide binding protein 3; P2RY12, purinergic receptor p2y12; PLP, myelin proteolipid protein; RPL19, 60S ribosomal L19; RT-qPCR, quantitative real-time reverse transcription polymerase chain reaction; S100B, S100 calcium binding protein B; TIMP2, tissue inhibitor of metalloproteinases 2; TMEM119, transmembrane protein 119; TNF- $\alpha$ , tumor necrosis factor alpha; TREM2, triggering receptor expressed on myeloid cells 2.

**Table S2.** List of miRNA sequences used in RT-qPCR.

| miRNA            | Target sequence (5'-3') |
|------------------|-------------------------|
| hsa miR-146a-5p  | UGAGAACUGAAUCCAUGGGUU   |
| mmu -miR-155-5p  | CTCAGAGAGGTGGAAGACCATGT |
| hsa miR-21-5p    | UAGCUUAUCAGACUGAUGUUGA  |
| hsa-miR-124-3p   | UAAGGCACGCGGUGAAUGCC    |
| hsa -miR-125b-5p | UCCCUGAGACCCUAACUUGUGA  |
| SNORD110         | Reference gene          |

miRNA, microRNA; mmu, mouse; hsa, human.

**Table S3.** List of antibodies used for immunohistochemistry (IHC) or western blot (WB).

|           | Antibodies                 | Source                             | Species | Dilution |        |
|-----------|----------------------------|------------------------------------|---------|----------|--------|
|           |                            |                                    |         | IHC      | WB     |
| Primary   | Anti- $\beta$ -actin       | Sigma, A5441                       | Mouse   | -        | 1:2500 |
|           | Anti-GFAP                  | NovoCastra, GFAP-GA5-6035278       | Mouse   | 1:100    | -      |
|           | Anti-GFAP                  | Sigma-Aldrich, G9269               | Rabbit  | -        | 1:500  |
|           | Anti-Iba1                  | Wako, 019-19741                    | Rabbit  | 1:250    | 1:500  |
|           | Anti-Neu N                 | Millipore, MAB377                  | Mouse   | 1:100    | 1:100  |
|           | Anti-S100B                 | AbCam, ab52642                     | Rabbit  |          | 1:1000 |
|           | Anti-Vimentin              | sc-32322, Santa Cruz Biotechnology | Mouse   | -        | 1:200  |
| Secondary | AlexaFluor 488 anti-mouse  | Invitrogen, A-10680                | Goat    | 1:500    | -      |
|           | AlexaFluor 594 anti-rabbit | Invitrogen, A-11012                | Goat    | 1:500    | -      |
|           | HRP anti-rabbit            | Santa Cruz Biotechnology, sc2357   | Mouse   | -        | 1:5000 |
|           | Mouse-IgG $\kappa$ BP-HRP  | Santa Cruz Biotechnology, sc516102 | -       | -        | 1:5000 |

GFAP, glial fibrillary acidic protein; HRP, horseradish peroxidase; Iba-1, ionized calcium-binding adapter molecule 1; NeuN, hexaribonucleotide binding protein 3; S100B, S100 calcium-binding protein B.

**Table S4.** Expression of genes, miRNAs and proteins from the muscle and lumbar spinal cord of mSOD1 mice injected with the vehicle or the secretome derived from anti-miR-124-treated mSOD1 MNs (mSOD1 + sec). Results are mean ( $\pm$  SEM) and expressed fold change *vs.* WT + vehicle. One-way ANOVA followed by multiple comparisons Bonferroni post hoc correction was used.

| Markers            | Fold change<br>(WT mice +<br>vehicle <i>vs.</i> WT<br>mice + vehicle<br>Mean $\pm$ SEM | Fold change<br>(mSOD1 mice +<br>vehicle <i>vs.</i> WT<br>mice + vehicle<br>Mean $\pm$ SEM | <i>p</i> values<br>( <i>vs.</i> WT<br>mice +<br>vehicle) | Fold change<br>(mSOD1 mice +<br>sec <i>vs.</i> WT mice +<br>vehicle)<br>Mean $\pm$ SEM | <i>p</i> values<br>( <i>vs.</i> WT<br>mice +<br>vehicle) | <i>p</i> values<br>( <i>vs.</i><br>mSOD1<br>mice +<br>vehicle) |
|--------------------|--|---|--|--|--|--|
| <b>Muscle</b>      |  |   |  |  |  |  |
| <b>Genes</b>       |  |   |  |  |  |  |
| NeuN               | 1.00 $\pm$ 0.03  | 0.45 $\pm$ 0.10   | 0.015  | 1.18 $\pm$ 0.12  | 0.863  | 0.003  |
| Synaptophysin      | 1.06 $\pm$ 0.16  | 0.51 $\pm$ 0.10   | 0.049  | 1.14 $\pm$ 0.14  | 0.973  | 0.024  |
| PSD-95             | 1.01 $\pm$ 0.11  | 0.23 $\pm$ 0.08   | <0.001   | 0.78 $\pm$ 0.06  | 0.365  | 0.011  |
| <b>Spinal cord</b> |  |   |  |  |  |  |
| <b>Genes</b>       |  |   |  |  |  |  |
| NeuN               | 1.01 $\pm$ 0.08  | 0.58 $\pm$ 0.03   | 0.004  | 0.80 $\pm$ 0.083   | 0.181  | 0.163  |
| Synaptophysin      | 0.97 $\pm$ 0.04  | 0.95 $\pm$ 0.03   | >0.999   | 0.94 $\pm$ 0.10  | >0.999   | >0.999   |
| PSD-95             | 1.00 $\pm$ 0.07  | 0.51 $\pm$ 0.06   | 0.008  | 0.70 $\pm$ 0.06  | 0.024  | 0.211  |
| Dynein             | 1.00 $\pm$ 0.05  | 0.56 $\pm$ 0.07   | 0.208  | 0.97 $\pm$ 0.17  | >0.999   | 0.166  |
| Kinesin            | 1.00 $\pm$ 0.02  | 0.72 $\pm$ 0.06   | >0.999   | 0.88 $\pm$ 0.19  | >0.999   | 0.648  |
| CX3CL1             | 1.00 $\pm$ 0.06  | 0.76 $\pm$ 0.04   | 0.032  | 0.73 $\pm$ 0.06  | 0.022  | >0.999   |
| MBP                | 1.00 $\pm$ 0.03  | 0.74 $\pm$ 0.08   | 0.019  | 1.16 $\pm$ 0.04  | 0.156  | <0.001   |
| PLP                | 1.00 $\pm$ 0.03  | 0.73 $\pm$ 0.06   | 0.006  | 1.07 $\pm$ 0.03  | 0.927  | <0.001   |
| GPR17              | 1.02 $\pm$ 0.13  | 2.53 $\pm$ 0.25   | 0.008  | 2.24 $\pm$ 0.34  | 0.038  | >0.999   |
| CX3CR1             | 1.01 $\pm$ 0.07  | 1.53 $\pm$ 0.11   | 0.011  | 1.50 $\pm$ 0.12  | 0.009  | >0.999   |
| Arginase 1         | 1.01 $\pm$ 0.08  | 0.69 $\pm$ 0.04   | 0.939  | 1.58 $\pm$ 0.32  | 0.221  | 0.042  |
| TMEM119            | 1.04 $\pm$ 0.17  | 2.28 $\pm$ 0.28   | 0.044  | 2.21 $\pm$ 0.35  | 0.059  | >0.999   |
| TIMP2              | 1.01 $\pm$ 0.07  | 1.49 $\pm$ 0.07   | 0.016  | 1.51 $\pm$ 0.14  | 0.011  | >0.999   |
| P2RY12             | 1.01 $\pm$ 0.07  | 0.73 $\pm$ 0.03   | 0.028  | 0.81 $\pm$ 0.03  | 0.121  | >0.999   |
| TREM2              | 1.03 $\pm$ 0.12  | 0.22 $\pm$ 0.07   | 0.004  | 0.69 $\pm$ 0.16  | 0.291  | 0.075  |
| MFG-E8             | 0.97 $\pm$ 0.04  | 0.95 $\pm$ 0.03   | 0.136  | 0.94 $\pm$ 0.10  | 0.549  | >0.999   |
| S100B              | 1.00 $\pm$ 0.05  | 1.02 $\pm$ 0.05   | >0.999   | 1.04 $\pm$ 0.06  | >0.999   | >0.999   |
| GFAP               | 1.01 $\pm$ 0.07  | 3.00 $\pm$ 0.58   | 0.003  | 1.49 $\pm$ 0.20  | 0.036  | >0.999   |
| CX43               | 1.00 $\pm$ 0.06  | 1.66 $\pm$ 0.11   | 0.002  | 1.26 $\pm$ 0.13  | 0.368  | 0.065  |
| TNF- $\alpha$      | 1.00 $\pm$ 0.04  | 2.54 $\pm$ 0.54   | 0.050  | 2.25 $\pm$ 0.38  | 0.117  | >0.999   |
| IL-10              | 1.01 $\pm$ 0.07  | 0.43 $\pm$ 0.08   | 0.023  | 1.46 $\pm$ 0.18  | 0.058  | <0.001   |
| IL-1 $\beta$       | 1.03 $\pm$ 0.11  | 1.16 $\pm$ 0.13   | >0.999   | 1.15 $\pm$ 0.09  | >0.999   | >0.999   |
| iNOS               | 1.02 $\pm$ 0.09  | 0.48 $\pm$ 0.09   | 0.053  | 1.48 $\pm$ 0.19  | 0.108  | <0.001   |
| <b>Proteins</b>    |  |   |  |  |  |  |
| NeuN               | 1.00 $\pm$ 0.12  | 0.34 $\pm$ 0.08   | 0.051  | 1.14 $\pm$ 0.23  | >0.999   | 0.014  |
| GFAP               | 1.00 $\pm$ 0.05  | 2.22 $\pm$ 0.55   | 0.263  | 1.54 $\pm$ 0.24  | >0.999   | 0.836  |
| S100B              | 1.00 $\pm$ 0.13  | 2.75 $\pm$ 0.84   | 0.113  | 1.50 $\pm$ 0.40  | >0.999   | 0.377  |

|               |             |             |       |             |        |        |
|---------------|-------------|-------------|-------|-------------|--------|--------|
| Vimentin      | 1.00 ± 0.14 | 2.13 ± 0.43 | 0.046 | 1.43 ± 0.07 | 0.845  | 0.297  |
| Iba-1         | 1.00 ± 0.08 | 1.65 ± 0.23 | 0.030 | 1.49 ± 0.16 | 0.132  | >0.999 |
| <b>miRNAs</b> |             |             |       |             |        |        |
| miR-124       | 1.00 ± 0.05 | 1.39 ± 0.03 | 0.003 | 1.08 ± 0.08 | >0.999 | 0.018  |
| miR-146a      | 1.01 ± 0.05 | 1.59 ± 0.28 | 0.121 | 1.42 ± 0.18 | 0.447  | >0.999 |
| miR-155       | 1.00 ± 0.05 | 2.06 ± 0.52 | 0.017 | 0.97 ± 0.11 | >0.999 | 0.017  |
| miR-21        | 1.00 ± 0.02 | 1.52 ± 0.20 | 0.053 | 1.23 ± 0.15 | 0.650  | 0.546  |
| miR-125b      | 1.00 ± 0.03 | 1.10 ± 0.06 | 0.738 | 1.15 ± 0.07 | 0.296  | >0.999 |

Results are mean (± SEM) and expressed fold change *vs.* WT + vehicle. One-way ANOVA followed by multiple comparisons Bonferroni post hoc correction was used. CX3CL1, C-X3-C motif chemokine ligand 1/fractalkine; CX3CR1, c-x3-c chemokine receptor 1; Cx43, connexin 43; GFAP, glial fibrillary acidic protein; GPR17, G protein-coupled receptor 17; Iba-1, ionized calcium-binding adaptor molecule 1; IL-10, interleukin 10; IL-1β, interleukin 1β; iNOS, inducible nitric oxide synthase; MBP, myelin basic protein; MFG-E8, milk fat globule-epidermal growth factor-factor 8; miRNA, microRNA; NeuN, hexaribonucleotide binding protein 3; P2RY12, purinergic receptor p2y12; PLP, myelin proteolipid protein; PSD-95, postsynaptic density protein 95; S100B, S100 calcium binding protein B; TIMP2, tissue inhibitor of metalloproteinases 2; TMEM119, transmembrane protein 119; TNF-α, tumour necrosis factor alpha TREM 2, triggering receptor expressed on myeloid cells 2.