**Supplementary Information**

# Type-dependent effects of nanoplastics on microglial activation and CXCR2-mediated chemotactic migration

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## Supplementary Materials and Methods

### Fourier-transform infrared spectroscopy (FTIR)

The chemical structures of nanoplastics were analyzed using Fourier-transform infrared spectroscopy (FTIR, Alpha-T, Bruker). FTIR spectra were obtained in ATR mode with a resolution of 4 $cm^{-1}$ and 64 scan times. The fluorescence intensity of three nanoplastics was measured using a microplate reader (Cytation5, BioTek). Fluorescence standard curves for each nanoplastic were obtained under the following excitation/emission conditions: 441/486 nm for PSNP, 540/580 nm for PPNP, 565/620 nm for PMMANP.

### Dynamic light scattering (DLS) analysis

DLS analysis was performed as previously described[1]. The hydrodynamic sizes and zeta potential values of these nanoplastics in distilled water and cell culture medium were measured using a particle size analyzer (Zetasizer Nano ZS, Malvern Instruments). To confirm the stability of nanoplastics (NPs) in the culture medium used in this study, the nanoplastics were analyzed using DLS in distilled water (DW) and under conditions equivalent to those in microglia cultures on days 0, 1, and 3.

### Cell viability analysis (MTT assay)

Potential cytotoxicity in microglia was measured using the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Primary rat microglia were plated in a 96-well cell culture plate at a density of $5 \times 10^4$ cells per well. Nanoplastics were added to each well at concentrations of 25, 50, 100, and 200 μg/ml and incubated for 24 hours. The nanoplastic-containing medium was then aspirated, and 100 μl of MTT solution (2 mg/ml) was added to the remaining microglia. The plate was incubated for 4 hours at 37℃ and 5% CO2. Formazan (reduced MTT) in the microglia was extracted by the incubation for 20 minutes at room temperature after adding 200 μl of dimethyl sulfoxide (DMSO, Sigma-aldrich). Optical density (OD) was measured at a wavelength of 570 nm using a microplate reader (VersaMax Absorbance Microplate Reader, Molecular Devices, San Jose, CA, USA). The data were normalized to the non-treated control values and expressed as percent viability.

### Nitrite secretion measurement (Griess assay)

Nitrite levels in the culture supernatant of primary rat microglia were measured using the PicoSens™ Griess Reagent

Assay Kit (BM-GRI-1000, BIOMAX, Guri-si, South Korea). Supernatants were collected 24 hours after nanoplastic exposure and centrifuged at 3,000 × g for 3 minutes to remove cells and debris. The assay was performed according to the manufacturer's instructions. Briefly, 50 µL of each supernatant sample was added to a 96-well plate, followed by the addition of 50 µL each of Solution I and Solution II. The plate was then incubated at room temperature for 10 minutes in the dark. Optical density (OD) was measured at 540 nm using a microplate reader. Nitrite concentrations were determined using a standard curve generated with the nitrite standards provided in the kit.

**Table S1. List of primer pairs for qRT-PCR**

| | Forward | Reverse |
|---|---|---|
| *Tnfa* | 5'-CGT CAG CCG ATT TGC CAT TT-3' | 5'-TCC CTC AGG GGT GTC CTT AG-3' |
| *Cd86* | 5'-AGA CAT GTG TAA CCT GCA CCA T-3' | 5'-GCC CGT GTC CTT GAT CTG AA-3' |
| *Arg1* | 5'-ATG AGC TCC AAG CCA AAG CCC ATA-3' | 5'-TTA TTT CGG TGG TTT AAG GTA GT-3' |
| *Igf-1* | 5'-TCT TCT ACC TGG CAC TCT GCT-3' | 5'-ACG AAC TGA AGA GCG TCC AC-3' |
| *CD206* | 5'-GAC GGA CGA GGA GTT CAT TAT AC-3' | 5'-GTT GGA GAG ATA GGC ACA GAA G-3' |
| *Tgfb1* | 5'-CAC TCC CGT GGC TTC TAG TG-3' | 5'-CTG GCG AGC CTT AGT TTG GA-3' |
| *Cxcr2* | 5'-CTG ACC CGC CCT TTA CTC TG-3' | 5'-CAG GGA GTT TCC CAC GAG AC-3' |
| *Cxcr3* | 5'-TGG GGA AAA CGA AAG CGA CT-3' | 5'-TCT GGG TGG CAT GCA CTA TG-3' |
| *Cxcl11* | 5'-TCC GTT TTG CCA GAT TGC AG-3' | 5'-CTT CTG AAT CCA ACC AGC GG-3' |
| *Iba1* | 5'-AGA GCA AGG ATT TGC AGG GAG-3' | 5'-CCA AGT TTC TCC AGC ATT CGC-3' |
| *Itgb4* | 5'-ACT GAG CAC CTG GTG AAT GG-3' | 5'-TTC CCA GAT AGG AGG GAG GC-3' |
| *Lamb1* | 5'-ACA CGA AGA AAA GAC GGG CA-3' | 5'-CCT GCA GGT GGC TGA CAA TA-3' |
| *Cxcl1* | 5'-ACT CAA GAA TGG TCG CGA GG-3' | 5'-ACG CCA TCG GTG CAA TCT AT-3' |
| *Cxcl2* | 5'-CGA CCC TAC CAA GGG TTG AC-3' | 5'-AGG TAC GAT CCA GGC TTC CT-3' |
| *Gapdh* | 5'-GCA TCT TCT TGT GCA GTG CC-3' | 5'-ACC AGC TTC CCA TTC TCA GC-3' |

**Table S2. Physicochemical characterization of three different types of nanoplastics**

| | PSNP | PPNP | PMMANP |
|---|---|---|---|
| **Manufacture** | Polyscience Inc. (PA, USA) | Dr. Jinyoung Jeong in KRIBB (Republic of Korea) | Poly An (Berlin, Germany) |
| **Functional group** | Plain | Plain | Plain |
| **Fluorescence condition** | Ex: 441 nm Em: 486 nm | Ex: 540 nm Em: 580 nm | Ex: 565 nm Em: 620 nm |
| **Density ($g/cm^3$)** | 0.96 ~ 1.05 | 0.855 ~ 0.946 | 1.18 |
| **Size (nm) by SEM** | 443.28 ± 16.41 | 480.68 ± 77.54 | 419.16 ± 35.24 |
| **Hydrodynamic size by DLS** | 488.7 ± 13.11 nm | 719.97 ± 35.36 nm | 482.77 ± 10.85 nm |
| **Zeta-potential** | -63.7 ± 1.17 mV | -55.1 ± 0.17 mV | -73.83 ± 28.74 mV |

## Supplementary Figures

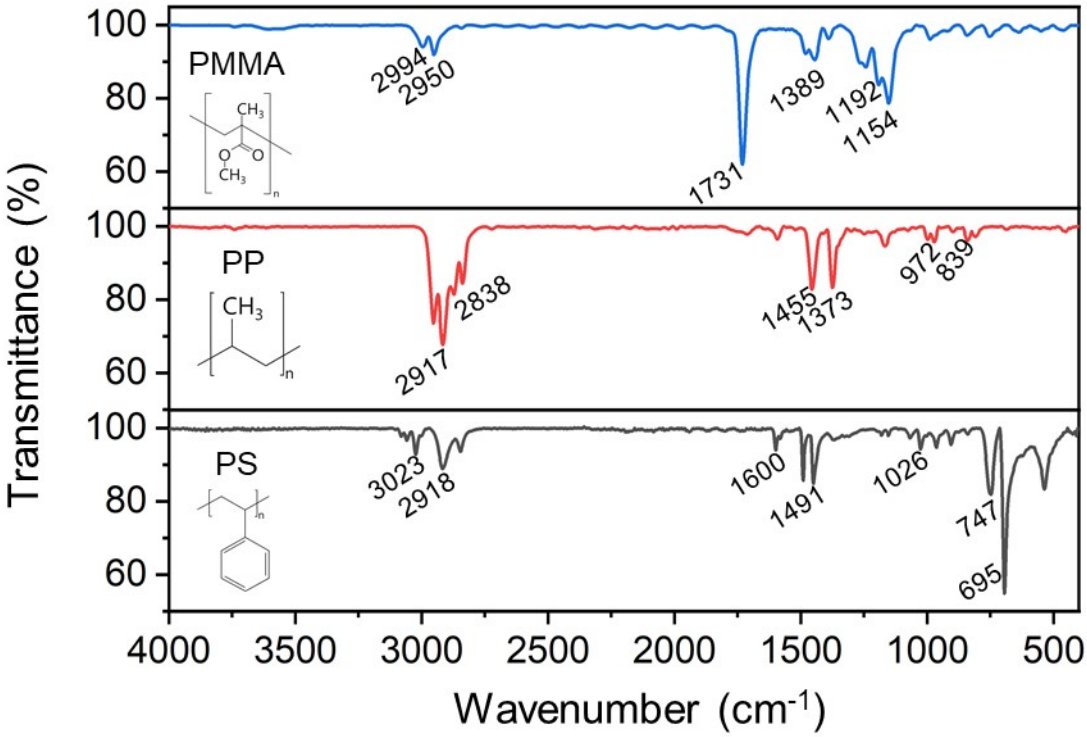


**Figure S1. FTIR spectra of three different types of nanoplastics (PS, PP, PMMA) measured by ATR mode.**

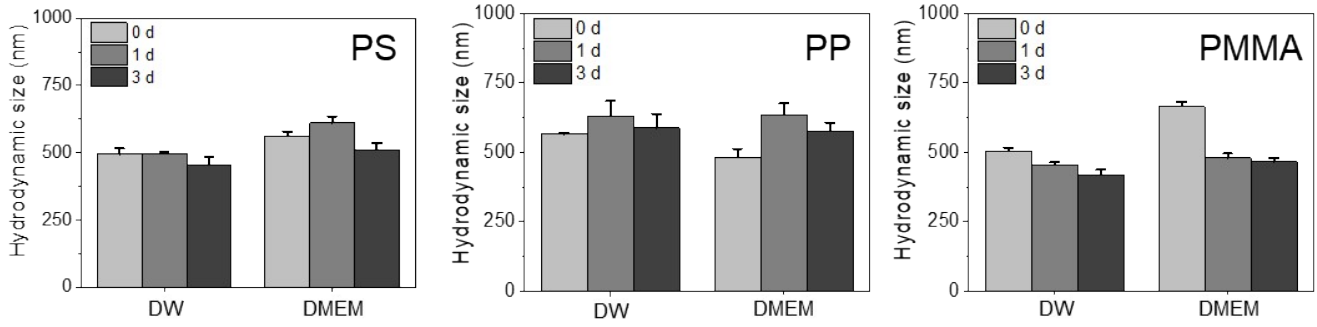


**Figure S2. Nanoplastic particles remain as single entities without aggregation in both water and culture condition.** DLS analysis data show the hydrodynamic sizes of three different nanoplastics (PSNP (PS), PPNP (PP) and PMMANP (PMMA)) in both distilled water and DMEM, the culture medium for microglia from day 0 to day 3. Values denote means± *SEMs*.

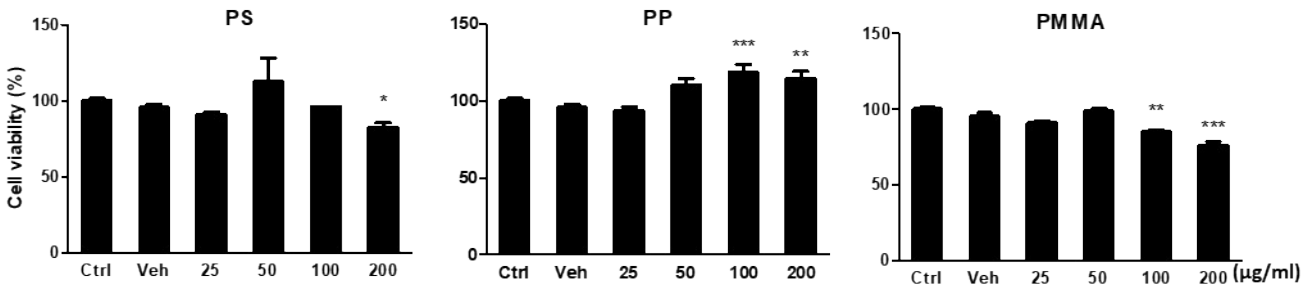


**Figure S3. No cytotoxicity was observed in microglia with nanoplastics at dosages ≤50 μg/ml.** MTT analysis data show the cell viability at 24 hours after the treatment of three different types of NPs (PSNP (PS), PPNP (PP) and PMMANP (PMMA)). Vehicle-treated microglia was used as a control (Veh). Values denote means ±*SEMs*. One-way ANOVA with Dunnett's post hoc test. *$p$<0.05, **$p$<0.005, ***$p$<0.0005.

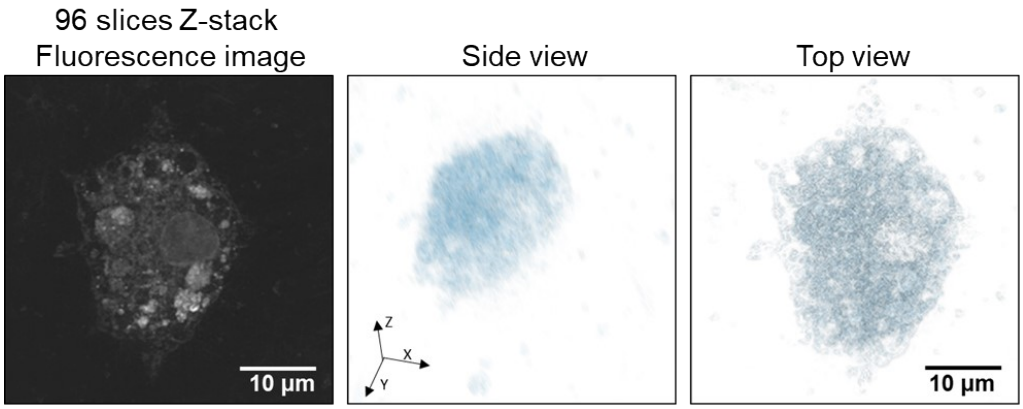


**Figure S4. No nanoplastic signal was observed in untreated microglia.** Panels show the fluorescent and optical diffraction tomographic images (both side and top views) of microglia without nanoplastic treatment. The RI value of the cytoplasm in microglia was 1.3384, which is relatively lower compared to the values in nanoplastic-treated cells (1.3405 ~ 1.3415). Scale bar: 10 μm

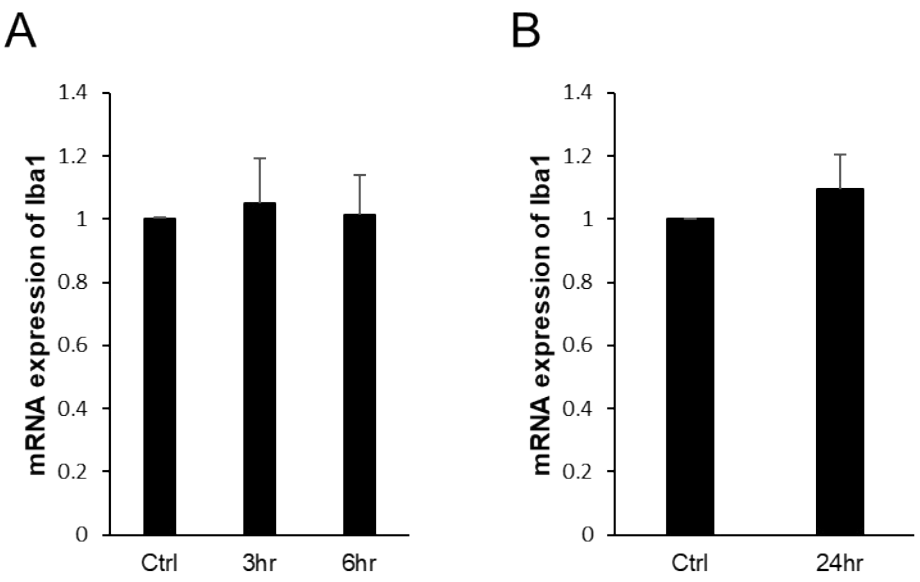


**Figure S5. Iba1 expression was not altered in PMMANP-exposed microglia.** qRT-PCR data show that the mRNA expression of *Iba1* was not altered by PMMANP (50 μg/ml) treatment in microglia. Values denote means ±*SEMs*.

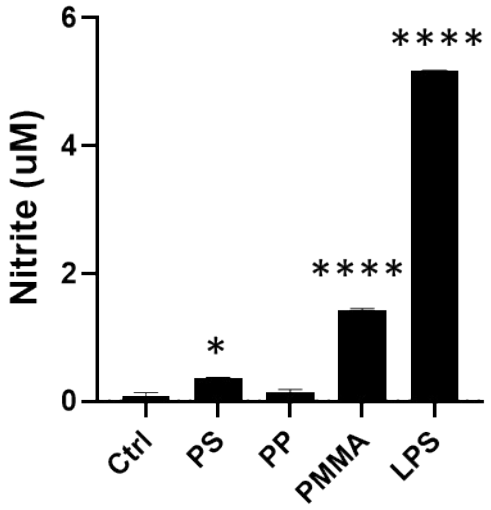


**Figure S6. Nitrite secretion varied depending on type of nanoplastic.** Griess assay data show an increase in nitrite secretion in the groups exposed to PSNP (PS) and PMMANP (PMMA). LPS-treated group was used as a positive control. Values denote means ±*SEMs*. Two-tail unpaired *t*-test *$p$<0.05, ****$p$<0.0001.

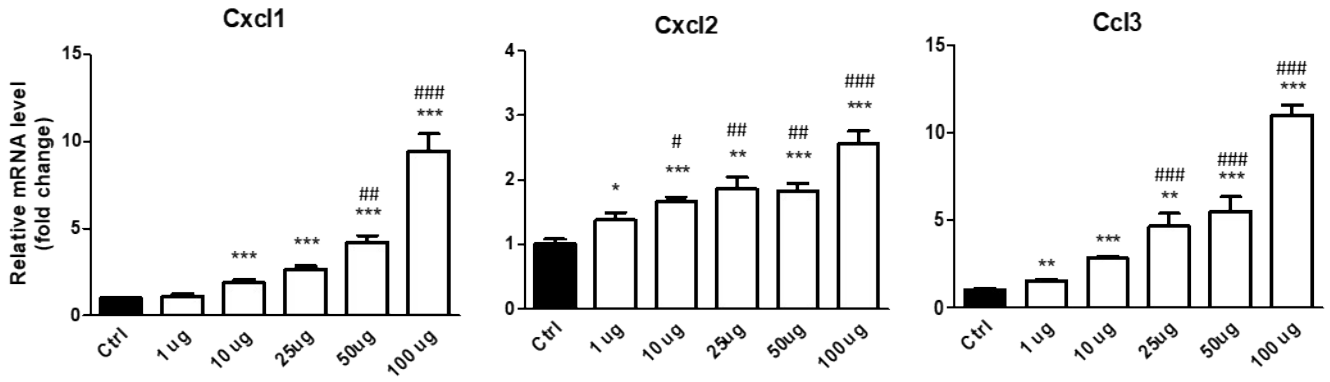


**Figure S7. Chemokine expression was increased by PMMANP in a dose-dependent manner in microglia.** qRT-PCR data show the increase in mRNA expression of chemokines (*Cxcl1, Cxcl2 and Ccl3*) in microglia at 3 hours after treatment with PMMANP (0-100 μg/ml). Values denote means ±*SEMs*. Unpaired t-test **p*<0.05, ***p*<0.005, ****p*<0.0005, compared to Ctrl. One-way ANOVA with Dunnett's post hoc test. #*p*<0.05, ##*p*<0.005, ###*p*<0.0005.

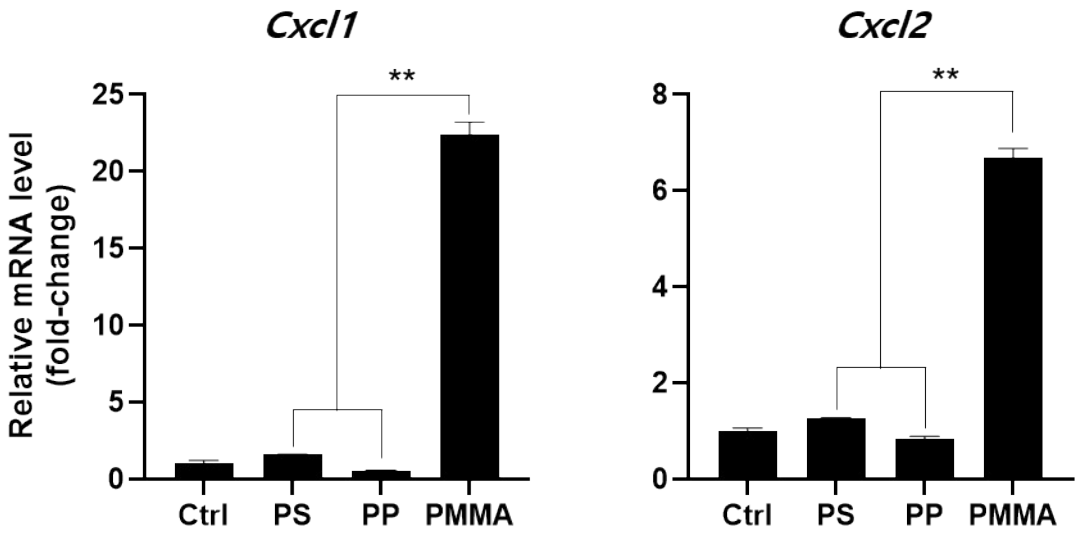


**Figure S8. The chemokine expression pattern was not affected by the fluorescence conjugation on the surface of the nanoplastics.** qRT-PCR data show that the mRNA expression levels of *Cxcl1* and *Cxcl2* were significantly higher in PMMA-treated microglia compared to PS- and PP-treated microglia, 24 hours after treatment with transparent nanoplastics (without fluorescence conjugation). Values denote means ±*SEMs*. Unpaired t-test ***p* <0.005, compared to PMMA group.

**Table S3. List of genes altered by PMMANP treatment in microglia: Selected genes based on RNA sequencing**

| ESG | Gene Symbol | CTRL Set1 | PMMA Set1 | CTRL Set2 | PMMA Set2 | Fold-change Set1 | Fold-change Set2 | Regulation |
|---|---|---|---|---|---|---|---|---|
| ENSRNOG00000063015 | . | 0.118 | 35.708 | 0.192 | 123.480 | 303.71 | 642.01 | Up |
| ENSRNOG00000066746 | . | 0.685 | 13.753 | 0.317 | 0.548 | 20.07 | 1.73 | Up |
| ENSRNOG00000008170 | Jph2 | 0.010 | 0.144 | 0.021 | 0.057 | 14.70 | 2.76 | Up |
| ENSRNOG00000039203 | AABR07040892.1 | 0.008 | 0.075 | 0.048 | 0.094 | 9.19 | 1.94 | Up |
| ENSRNOG00000069262 | . | 0.023 | 0.164 | 0.033 | 0.058 | 7.21 | 1.75 | Up |
| ENSRNOG00000063843 | . | 0.053 | 0.354 | 0.100 | 0.369 | 6.62 | 3.68 | Up |
| ENSRNOG00000067606 | . | 0.200 | 1.198 | 0.186 | 0.570 | 5.98 | 3.07 | Up |
| ENSRNOG00000033434 | Casp12 | 0.019 | 0.111 | 0.152 | 0.402 | 5.79 | 2.65 | Up |
| ENSRNOG00000063618 | Cxcr2 | 0.033 | 0.172 | 0.150 | 0.314 | 5.15 | 2.10 | Up |
| ENSRNOG00000007690 | Cmpk2 | 17.022 | 85.538 | 4.632 | 8.528 | 5.03 | 1.84 | Up |
| ENSRNOG00000022298 | Cxcl11 | 4.879 | 21.399 | 0.065 | 0.490 | 4.39 | 7.59 | Up |
| ENSRNOG00000022839 | Ifit3 | 150.082 | 636.901 | 42.111 | 72.016 | 4.24 | 1.71 | Up |
| ENSRNOG00000009919 | Acod1 | 5.071 | 21.008 | 1.102 | 3.060 | 4.14 | 2.78 | Up |
| ENSRNOG00000069527 | Isg15 | 97.266 | 385.197 | 175.454 | 367.527 | 3.96 | 2.09 | Up |
| ENSRNOG00000023410 | Apol9a | 4.730 | 18.594 | 6.024 | 15.179 | 3.93 | 2.52 | Up |
| ENSRNOG00000001976 | Tmprss2 | 0.720 | 2.812 | 0.756 | 1.691 | 3.90 | 2.24 | Up |
| ENSRNOG00000010440 | Gnal | 0.072 | 0.278 | 0.063 | 0.171 | 3.87 | 2.70 | Up |
| ENSRNOG00000061739 | Klrk1 | 0.480 | 1.713 | 0.861 | 1.955 | 3.57 | 2.27 | Up |
| ENSRNOG00000059207 | Oas3 | 1.430 | 5.062 | 0.770 | 1.396 | 3.54 | 1.81 | Up |
| ENSRNOG00000047697 | Ggt1 | 0.076 | 0.255 | 0.018 | 0.056 | 3.35 | 3.18 | Up |
| ENSRNOG00000015078 | Ifitm3 | 3.937 | 12.848 | 1.896 | 4.780 | 3.26 | 2.52 | Up |
| ENSRNOG00000068063 | Rnaseh2a | 1.138 | 3.696 | 1.199 | 2.212 | 3.25 | 1.84 | Up |
| ENSRNOG00000069361 | Pde6g | 0.061 | 0.195 | 0.467 | 0.968 | 3.22 | 2.07 | Up |
| ENSRNOG00000001187 | Oasl | 54.657 | 172.533 | 45.661 | 82.495 | 3.16 | 1.81 | Up |
| ENSRNOG00000052981 | AABR07058464.1 | 3.594 | 11.200 | 8.723 | 23.406 | 3.12 | 2.68 | Up |
| ENSRNOG00000069830 | . | 0.009 | 0.026 | 0.004 | 0.008 | 3.06 | 1.94 | Up |
| ENSRNOG00000068341 | . | 0.078 | 0.231 | 0.074 | 0.134 | 2.97 | 1.80 | Up |
| ENSRNOG00000037718 | Cfap52 | 0.074 | 0.218 | 0.039 | 0.142 | 2.95 | 3.64 | Up |
| ENSRNOG00000023614 | Hsh2d | 2.474 | 7.136 | 1.180 | 2.017 | 2.88 | 1.71 | Up |
| ENSRNOG00000013872 | P2ry14 | 2.384 | 6.817 | 1.235 | 2.165 | 2.86 | 1.75 | Up |
| ENSRNOG00000059097 | AABR07025140.1 | 19.739 | 56.096 | 8.156 | 18.617 | 2.84 | 2.28 | Up |
| ENSRNOG00000006314 | Zbp1 | 27.935 | 74.047 | 26.188 | 46.401 | 2.65 | 1.77 | Up |
| ENSRNOG00000063679 | . | 8.399 | 22.094 | 20.770 | 60.346 | 2.63 | 2.91 | Up |
| ENSRNOG00000056783 | Cd69 | 0.528 | 1.369 | 0.051 | 0.131 | 2.60 | 2.59 | Up |
| ENSRNOG00000037167 | Rtp3 | 0.898 | 2.182 | 0.067 | 0.173 | 2.43 | 2.58 | Up |
| ENSRNOG00000037814 | Cxcl17 | 14.754 | 35.654 | 5.576 | 10.590 | 2.42 | 1.90 | Up |
| ENSRNOG00000031443 | Havcr2 | 1.415 | 3.308 | 0.102 | 0.286 | 2.34 | 2.80 | Up |
| ENSRNOG00000017414 | Irf7 | 80.168 | 182.640 | 81.655 | 194.205 | 2.28 | 2.38 | Up |
| ENSRNOG00000013324 | Cdh5 | 1.172 | 2.596 | 0.568 | 0.979 | 2.21 | 1.72 | Up |
| ENSRNOG00000008919 | Arpp21 | 0.077 | 0.170 | 0.013 | 0.082 | 2.21 | 6.20 | Up |
| ENSRNOG00000068024 | B3gnt8 | 0.057 | 0.126 | 0.008 | 0.132 | 2.20 | 16.76 | Up |
| ENSRNOG00000013975 | Acat2l1 | 0.019 | 0.041 | 0.028 | 0.158 | 2.18 | 5.73 | Up |
| ENSRNOG00000009434 | RGD1310507 | 0.052 | 0.112 | 0.036 | 0.072 | 2.15 | 1.98 | Up |
| ENSRNOG00000010813 | Tspan14 | 14.881 | 31.926 | 6.334 | 20.988 | 2.15 | 3.31 | Up |
| ENSRNOG00000039829 | Rpp14 | 0.517 | 1.101 | 0.021 | 3.919 | 2.13 | 189.35 | Up |
| ENSRNOG00000033984 | Ifnlr1 | 0.169 | 0.355 | 0.080 | 0.197 | 2.10 | 2.45 | Up |
| ENSRNOG00000020095 | Pcdhb3 | 0.166 | 0.346 | 0.013 | 0.025 | 2.08 | 1.90 | Up |
| ENSRNOG00000033090 | Ltbp1 | 0.082 | 0.167 | 0.016 | 0.041 | 2.03 | 2.57 | Up |
| ENSRNOG00000002217 | Plac8 | 3.732 | 7.572 | 0.483 | 1.408 | 2.03 | 2.92 | Up |
| ENSRNOG00000022392 | Hspb8 | 0.206 | 0.415 | 0.122 | 0.328 | 2.01 | 2.70 | Up |
| ENSRNOG00000066766 | . | 0.206 | 0.414 | 0.095 | 0.238 | 2.01 | 2.50 | Up |
| ENSRNOG00000017684 | Fbxl22 | 0.096 | 0.192 | 0.123 | 0.213 | 2.00 | 1.74 | Up |
| ENSRNOG00000055769 | AABR07054286.1 | 0.084 | 0.164 | 0.041 | 0.084 | 1.96 | 2.02 | Up |
| ENSRNOG00000017762 | Cdhr5 | 0.118 | 0.227 | 0.040 | 0.130 | 1.92 | 3.26 | Up |
| ENSRNOG00000033444 | F10 | 24.834 | 47.678 | 15.195 | 27.727 | 1.92 | 1.82 | Up |
| ENSRNOG00000008775 | Lrguk | 0.053 | 0.100 | 0.022 | 0.043 | 1.91 | 1.94 | Up |
| ENSRNOG00000021719 | Slfn5 | 0.921 | 1.743 | 0.377 | 0.679 | 1.89 | 1.80 | Up |
| ENSRNOG00000003480 | Aim2 | 4.475 | 8.417 | 10.842 | 20.054 | 1.88 | 1.85 | Up |
| ENSRNOG00000020942 | Plekha4 | 0.137 | 0.250 | 0.155 | 0.289 | 1.82 | 1.87 | Up |
| ENSRNOG00000019734 | Mrpl14 | 3.913 | 7.083 | 4.077 | 13.923 | 1.81 | 3.42 | Up |
| ENSRNOG00000011316 | Fam167a | 0.248 | 0.447 | 0.050 | 0.116 | 1.80 | 2.32 | Up |
| ENSRNOG00000008012 | Abcb1b | 0.303 | 0.545 | 0.079 | 0.175 | 1.80 | 2.22 | Up |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ENSRNOG00000026607 | Tnfsf18 | 1.292 | 2.281 | 0.381 | 0.664 | 1.77 | 1.74 | Up |
| ENSRNOG00000029500 | Tapbp | 35.841 | 63.201 | 9.693 | 69.263 | 1.76 | 7.15 | Up |
| ENSRNOG00000036827 | Ppp1r1a | 0.406 | 0.711 | 0.308 | 0.806 | 1.75 | 2.62 | Up |
| ENSRNOG00000008151 | Plscr4 | 0.358 | 0.624 | 0.118 | 0.216 | 1.74 | 1.82 | Up |
| ENSRNOG00000019622 | Ackr3 | 0.456 | 0.794 | 0.009 | 0.022 | 1.74 | 2.42 | Up |
| ENSRNOG00000012415 | Mpc1 | 40.839 | 70.168 | 18.120 | 53.400 | 1.72 | 2.95 | Up |
| ENSRNOG00000011107 | Pcsk1 | 0.130 | 0.222 | 0.035 | 0.102 | 1.71 | 2.95 | Up |
| ENSRNOG00000018656 | Ampd1 | 0.186 | 0.318 | 0.082 | 0.310 | 1.71 | 3.78 | Up |
| ENSRNOG00000069312 | . | 0.109 | 0.185 | 0.045 | 0.106 | 1.70 | 2.34 | Up |
| ENSRNOG00000068757 | . | 0.462 | 0.051 | 0.196 | 0.047 | 9.07 | 4.20 | Down |
| ENSRNOG00000001869 | Rab44 | 0.077 | 0.010 | 0.046 | 0.024 | 7.45 | 1.95 | Down |
| ENSRNOG00000011100 | AABR07040947.1 | 61.578 | 10.124 | 22.636 | 5.372 | 6.08 | 4.21 | Down |
| ENSRNOG00000024456 | Radil | 0.175 | 0.040 | 0.145 | 0.082 | 4.37 | 1.78 | Down |
| ENSRNOG00000020355 | Twist2 | 0.518 | 0.138 | 0.126 | 0.063 | 3.75 | 2.00 | Down |
| ENSRNOG00000070875 | Nat8f4 | 0.144 | 0.041 | 0.042 | 0.024 | 3.51 | 1.75 | Down |
| ENSRNOG00000002110 | Fam114a1l1 | 0.088 | 0.025 | 0.046 | 0.013 | 3.49 | 3.45 | Down |
| ENSRNOG00000012303 | Apobec2 | 0.739 | 0.221 | 0.201 | 0.074 | 3.34 | 2.70 | Down |
| ENSRNOG00000000975 | Mcoln1 | 29.147 | 8.845 | 9.883 | 4.197 | 3.30 | 2.35 | Down |
| ENSRNOG00000030321 | . | 0.040 | 0.014 | 0.122 | 0.038 | 2.95 | 3.21 | Down |
| ENSRNOG00000010158 | Magel2 | 0.086 | 0.030 | 0.079 | 0.042 | 2.89 | 1.88 | Down |
| ENSRNOG00000017369 | Mustn1 | 0.154 | 0.058 | 0.782 | 0.398 | 2.66 | 1.97 | Down |
| ENSRNOG00000005404 | Rasgrp1 | 0.137 | 0.054 | 0.067 | 0.020 | 2.54 | 3.32 | Down |
| ENSRNOG00000015376 | Npas1 | 0.632 | 0.256 | 0.113 | 0.060 | 2.46 | 1.87 | Down |
| ENSRNOG00000042496 | Cyp4f5 | 0.550 | 0.226 | 0.177 | 0.075 | 2.44 | 2.35 | Down |
| ENSRNOG00000005678 | Lamb1 | 0.146 | 0.060 | 0.077 | 0.044 | 2.43 | 1.76 | Down |
| ENSRNOG00000005109 | Rprm | 0.317 | 0.132 | 0.093 | 0.029 | 2.40 | 3.19 | Down |
| ENSRNOG00000025730 | Armcx3 | 10.996 | 4.789 | 3.171 | 0.730 | 2.30 | 4.34 | Down |
| ENSRNOG00000050979 | Ubap1l | 0.342 | 0.150 | 0.916 | 0.534 | 2.28 | 1.72 | Down |
| ENSRNOG00000057703 | Cabp7 | 0.216 | 0.095 | 0.291 | 0.094 | 2.27 | 3.10 | Down |
| ENSRNOG00000009032 | Ttll3 | 0.165 | 0.075 | 0.449 | 0.234 | 2.20 | 1.92 | Down |
| ENSRNOG00000066473 | . | 0.566 | 0.262 | 0.876 | 0.445 | 2.16 | 1.97 | Down |
| ENSRNOG00000057044 | Garnl3 | 0.335 | 0.157 | 0.310 | 0.171 | 2.13 | 1.81 | Down |
| ENSRNOG00000049235 | Arl16 | 8.941 | 4.275 | 4.266 | 2.003 | 2.09 | 2.13 | Down |
| ENSRNOG00000007422 | Vav2 | 16.461 | 7.984 | 8.860 | 1.145 | 2.06 | 7.74 | Down |
| ENSRNOG00000067655 | Aldoa | 0.194 | 0.097 | 62.298 | 0.158 | 2.00 | 394.90 | Down |
| ENSRNOG00000069173 | RGD1563285 | 0.082 | 0.042 | 0.122 | 0.071 | 1.97 | 1.71 | Down |
| ENSRNOG00000026569 | Zfp943 | 1.565 | 0.796 | 2.742 | 0.638 | 1.97 | 4.30 | Down |
| ENSRNOG00000026974 | Dbndd1 | 0.420 | 0.215 | 0.082 | 0.043 | 1.95 | 1.92 | Down |
| ENSRNOG00000031607 | . | 0.115 | 0.059 | 0.079 | 0.011 | 1.94 | 7.20 | Down |
| ENSRNOG00000009565 | Pdk4 | 2.315 | 1.225 | 0.331 | 0.133 | 1.89 | 2.48 | Down |
| ENSRNOG00000005580 | Itgb4 | 0.019 | 0.010 | 0.093 | 0.021 | 1.87 | 4.52 | Down |
| ENSRNOG00000071190 | Pspn | 8.515 | 4.566 | 6.823 | 2.991 | 1.86 | 2.28 | Down |
| ENSRNOG00000025235 | Tmem130 | 0.224 | 0.122 | 0.092 | 0.043 | 1.83 | 2.15 | Down |
| ENSRNOG00000063309 | . | 3.926 | 2.179 | 1.583 | 0.902 | 1.80 | 1.75 | Down |
| ENSRNOG00000017568 | Rit2 | 0.766 | 0.430 | 0.148 | 0.067 | 1.78 | 2.19 | Down |
| ENSRNOG00000011112 | Fam161b | 0.533 | 0.299 | 0.377 | 0.193 | 1.78 | 1.95 | Down |
| ENSRNOG00000010680 | Med12l | 2.140 | 1.211 | 0.170 | 0.049 | 1.77 | 3.51 | Down |
| ENSRNOG00000017409 | Wnt6 | 0.247 | 0.140 | 0.256 | 0.058 | 1.76 | 4.41 | Down |
| ENSRNOG00000014285 | Ssh2 | 13.549 | 7.706 | 1.715 | 0.895 | 1.76 | 1.92 | Down |
| ENSRNOG00000007775 | Cmpk1 | 47.924 | 27.476 | 10.655 | 6.035 | 1.74 | 1.77 | Down |
| ENSRNOG00000008025 | Bend5 | 0.510 | 0.294 | 0.108 | 0.036 | 1.73 | 2.95 | Down |
| ENSRNOG00000066458 | Sco2 | 0.936 | 0.540 | 0.550 | 0.107 | 1.73 | 5.12 | Down |
| ENSRNOG00000014970 | Kif17 | 1.553 | 0.897 | 0.320 | 0.143 | 1.73 | 2.24 | Down |
| ENSRNOG00000052204 | Tbc1d24 | 10.719 | 6.211 | 2.154 | 0.676 | 1.73 | 3.19 | Down |

**Table S4. List of altered cytokines/chemokines by PMMANP: Selected genes based on RNA sequencing**

| | Gene ID | Set1 | | | | Set 2 | | | | Description |
|---|---|---|---|---|---|---|---|---|---|---|
| | | FPKM | | | Fold-Change (PMMA/Ctrl) | FPKM | | | Fold-Change (PMMA/Ctrl) | |
| | | Ctrl | PMMA | LPS (+ control) | | Ctrl | PMMA | LPS (+control) | | |
| | *Cxcl1* | 5.988834 | 8.484291 | 1400.01 | 1.416685 | 3.842628 | 5.474608 | 4047.949 | 1.424704 | C-X-C motif chemokine ligand 1 |
| | *Cxcl2* | 15.86808 | 25.9424 | 2292.768 | 1.63488 | 12.85391 | 17.74846 | 6246.355 | 1.380783 | C-X-C motif chemokine ligand 2 |
| | **Gene ID** | **Set1** | | | | **Set 2** | | | | **Description** |
| | | **FPKM** | | | **Fold-Change (PMMA/Ctrl)** | **FPKM** | | | **Fold-Change (PMMA/Ctrl)** | |
| | | **Ctrl** | **PMMA** | **LPS** | | **Ctrl** | **PMMA** | **LPS** | | |
| **Pro-inflammatory cytokine related genes** | *Ifnlr1* | 0.168917 | 0.35509 | 1.129935 | 2.102157 | 0.080178 | 0.19666 | 1.933122 | 2.452793 | Interferon Lambda Receptor 1 |
| | *Tnfrsf14* | 3.083877 | 6.726854 | 13.78447 | 2.181298 | 5.692422 | 7.406323 | 23.10981 | 1.301085 | TNF Receptor Superfamily Member 14 |
| | *Tnfsf18* | 1.29183 | 2.281105 | 57.83685 | 1.765793 | 0.381201 | 0.664241 | 5.4509 | 1.742495 | TNF Receptor Superfamily Member 18 |
| | *Tnfsf9* | 22.58026 | 33.23229 | 19.03302 | 1.471741 | 10.13394 | 13.94296 | 25.64127 | 1.375868 | TNF Receptor Superfamily Member 9 |
| | *Il1rn* | 2.588995 | 10.87644 | 67.69352 | 4.201026 | 31.89182 | 42.03273 | 65.91571 | 1.317978 | Interleukin-1 receptor antagonist |
| | *Il2rg* | 3.834681 | 5.402273 | 19.42031 | 1.408793 | 5.404174 | 8.11291 | 29.26771 | 1.50123 | interleukin 2 receptor subunit gamma |
| | *Cd86* | 30.20556 | 39.45837 | 348.8238 | 1.306328 | 8.431056 | 14.35548 | 53.17583 | 1.702691 | CD86 |
| **Anti-inflammatory cytokine related genes** | *Tgfa* | 10.78784 | 8.444553 | 4.160602 | 0.782784 | 0.942886 | 0.863273 | 0.383096 | 0.915565 | Transforming growth factor alpha |
| | *Tgfb1* | 113.515 | 130.8935 | 76.18525 | 1.153094 | 243.8807 | 279.513 | 257.1224 | 1.146106 | Transforming growth factor beta 1 |
| | *Tgfb1i1* | 0.879787 | 0.700168 | 1.914367 | 0.795838 | 0.631115 | 0.540281 | 0.72327 | 0.856074 | Transforming Growth Factor Beta 1 Induced Transcript 1 |
| | *Tgfb2* | 4.225731 | 3.561601 | 1.121313 | 0.842837 | 3.259324 | 3.256929 | 0.357096 | 0.999265 | Transforming growth factor beta 2 |
| | *Tgfbi* | 0.049483 | 0.053127 | 0.02778 | 1.073641 | 0.020915 | 0.031605 | 0.019497 | 1.511116 | Transforming growth factor beta induced |
| | *Tgfbr1* | 90.0442 | 77.73358 | 7.981473 | 0.863283 | 23.86431 | 20.78823 | 3.511771 | 0.871101 | transforming growth factor beta receptor 1 |
| | *Tgfbr2* | 100.4536 | 97.87216 | 34.31507 | 0.974302 | 36.88284 | 35.74614 | 38.66199 | 0.969181 | transforming growth factor beta receptor 2 |
| | *Tgfbr3* | 7.519946 | 5.691814 | 4.792994 | 0.756896 | 0.096629 | 0.075716 | 0.088091 | 0.783574 | transforming growth factor beta receptor 3 |

**Reference**

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