|              | • ·            |                       |                         |
|--------------|----------------|-----------------------|-------------------------|
| Gene         | Accession      | Forward               | Reverse                 |
| PPARy        | NM_001308352.1 | GACGCGGAAGAAGAGACCTG  | GGAATGCGAGTGGTCTTCCA    |
| PPARd        | NM_011145.3    | ATCGTCAACAAAGACGGGCT  | GCTTCTACCTGGGGCACATT    |
| RXRA         | NM_011305.3    | CCAAACATTTCCTGCCGCTC  | AGGGTCATTTGGTGAGCTGG    |
| NR1H3 (LXRA) | NM_013839.4    | AGTTAGTCTGGTGGGGAAGC  | CAACTCCGTTGCAGAATCAGG   |
| ABCA1        | NM_013454.3    | TCCTTGGGGACAGAATTGCC  | GCGTGTCACTTTCATGGTCG    |
| ABCG1        | NM_009593.2    | CCTGCCTCCTCTTCTACCCT  | TGCCTTGGGTTTGGGTTTCT    |
| SCARB1       | NM_016741.2    | AGCCAAGCTATAGGGTCCTG  | AGATCCGTCCTCTGTGGGAA    |
| SCARA2       | NM_010766.3    | CGAATCTTTCCAACGCGTCC  | TCTCTGTGCCCCGACAATTC    |
| CCL2         | NM_011333.3    | CTGCTGTTCACAGTTGCCG   | GCACAGACCTCTCTCTGAGC    |
| CCL3         | NM_011337.2    | TACAAGCAGCAGCGAGTACC  | GAGCAAAGGCTGCTGGTTTC    |
| HMG-CoAR     | NM_008255.2    | ACGATCCTTCCTTATTGGCGG | CACAGTCCTTGGATCCTCCG    |
| ELOVL1       | NC_000070      | CCTGGTTTCCACTGAGTCCT  | ACCCCATCAGAGGGTAGCTT    |
| ELOVL2       | NM_019423.2    | GAAGGTGATGTCCGGGTAGC  | CATGGACGCGTGGTGATAGA    |
| ELOVL3       | NM_007703.2    | TACTTCTTTGGCTCTCGCCC  | AGCTTACCCAGTACTCCTCCA   |
| ELOVL4       | NM_148941.2    | CTGGAGGCCAAGCGTTTTTC  | ATGGTCACGTGGAACTGGAC    |
| ELOVL5       | NM_134255.3    | CAGCTTGCTTCTGTTCCCG   | CTTTGACTCTTGTATCTCGGGG  |
| ELOVL6       | NM_130450.2    | CACCCGAACTAGGTGACACG  | CCGCAAGGCGTAGTAAGAGT    |
| ELOVL7       | NM_029001.5    | GAGAACCGGAAGCCCTTTGA  | CAGGTGTGCACCATCCTCAT    |
| FADS1        | NM_146094.2    | CGCCAAACGCGCTACTTTAC  | CCACAAAAGGATCCGTGGCA    |
| FADS2        | NM_019699.1    | CAGCCCCTTGAGTATGGCAA  | TAGTAGCTGATGGCCCAAGC    |
| DEGS1        | NM_007853.4    | GCAGAGCGGGTCCACAG     | TACTTTGCTAAGATCTCCTTGCG |
|              |                |                       |                         |

**Supplementary Table 1** | Forward and reverse primer sequences by gene for qPCR.

| D۸ | 14:0/16:0 | 14:0/18:1 | 16:0/18:1 | 16:1/18:1  | 18:0/20:1 | 18:0/20:2 | 18:0/22:4 |
|----|-----------|-----------|-----------|------------|-----------|-----------|-----------|
| PA | 14:0/16:1 | 16:0/16:1 | 16:0/20:1 | 16:1e/18:1 | 18:1/18:1 | 18:0/20:3 | 18:0/22:5 |
| РС | 14:0/16:0 | 16:0/20:4 | 16:0/22:4 | 16:1/20:4  | 18:0/22:5 | 18:0/16:0 | 18:1/16:0 |
|    | 14:0/18:0 | 16:0/22:4 | 16:0/22:5 | 16:1/22:4  | 18:0/22:6 | 18:0/18:0 | 18:1/18:0 |
|    | 14:0/18:2 | 16:1/18:2 | 16:0/22:6 | 16:1/22:5  | 18:1/18:2 | 18:0/18:2 | 18:1/18:2 |
|    | 16:0/16:0 | 16:0/14:0 | 16:1/14:0 | 16:1/22:6  | 18:1/18:3 | 18:0/20:1 | 18:1/20:2 |
|    | 16:0/18:0 | 16:0/16:0 | 16:1/16:0 | 18:0/18:2  | 18:1/20:2 | 18:0/20:2 | 18:1/20:3 |
|    | 16:0/18:2 | 16:0/18:2 | 16:1/18:0 | 18:0/20:1  | 18:1/20:3 | 18:0/20:3 | 18:1/20:4 |
|    | 16:0/18:3 | 16:0/20:1 | 16:1/18:2 | 18:0/20:2  | 18:1/22:4 | 18:0/20:4 | 18:1/22:4 |
|    | 16:0/20:1 | 16:0/20:2 | 16:1/20:1 | 18:0/20:3  | 18:2/18:2 | 18:0/22:4 | 18:1/22:6 |
|    | 16:0/20:2 | 16:0/20:3 | 16:1/20:2 | 18:0/20:4  | 18:2/20:1 | 18:0/22:5 | 20:1/20:4 |
|    | 16:0/20:3 | 16:0/20:4 | 16:1/20:3 | 18:0/22:4  | 18:0/14:0 | 18:0/22:6 | 20:1/22:5 |
| PG | 14:0/18:2 | 16:0/20:4 | 18:0/20:1 | 18:0/22:6  | 18:1/20:4 | 18:2/20:2 | 18:0/18:1 |
|    | 16:0/18:2 | 16:1/18:2 | 18:0/20:2 | 18:1/18:2  | 18:1/22:5 | 18:2/20:3 | 18:1/16:0 |
|    | 16:0/20:1 | 18:0/18:0 | 18:0/20:3 | 18:1/20:2  | 18:2/18:2 | 18:2/20:4 | 18:1/18:0 |
|    | 16:0/20:2 | 18:0/18:1 | 18:0/20:4 | 18:1/20:3  | 18:2/20:1 | 18:0/16:0 | 18:1/18:2 |
|    | 16:0/20:3 | 18:0/18:2 | 18:0/22:5 |            |           |           | 1.0       |
| PI | 14:0/18:2 | 16:0/18:2 | 16:1/18:0 | 18:0/18:2  | 18:0/18:1 | 18:0/20:1 | 18:1/20:1 |
|    | 14:0/20:4 | 16:0/22:4 | 16:1/18:2 | 16:1/18:1  | 18:1/18:2 | 18:0/20:2 | 18:1/16:0 |
|    | 14:0/22:5 | 16:0/18:1 | 16:0/18:1 | 16:1/18:2  | 18:0/18:0 | 18:1/18:1 | 18:1/18:1 |
|    | 14:0/22:6 | 16:0/16:0 |           |            |           |           |           |
| PS | 14:0/16:0 | 16:0/18:1 | 16:1/18:1 | 18:0/20:2  | 18:0/18:2 | 18:0/22:4 | 18:1/20:1 |
|    | 14:0/18:1 | 16:1/16:1 | 16:1/20:1 | 18:0/20:3  | 18:0/20:3 | 18:1/20:4 | 18:1/18:1 |
|    | 16:0/16:1 | 16:1/18:0 | 18:0/18:2 | 18:0/22:4  | 18:0/20:4 | 18:1/18:1 |           |
| PE | 14:0/18:2 | 16:0/22:6 | 16:1/14:0 | 16:1/22:6  | 18:0/22:6 | 18:1/18:3 | 18:1/22:6 |
|    | 14:0/20:4 | 16:0/16:1 | 16:1/16:1 | 16:1/22:6  | 18:0/20:4 | 18:1/20:4 | 18:2/20:3 |
|    | 14:0/22:5 | 16:0/14:0 | 16:1/18:0 | 18:0/18:2  | 18:0/22:4 | 18:1/22:4 | 18:2/20:4 |
|    | 16:0/18:2 | 16:0/16:1 | 16:1/18:1 | 18:0/18:3  | 18:0/22:5 | 18:1/22:6 | 18:2/22:4 |
|    | 16:0/18:3 | 16:0/22:4 | 16:1/20:1 | 18:0/20:3  | 18:0/22:6 | 18:1/20:2 | 18:2/22:5 |
|    | 16:0/20:3 | 16:0/22:5 | 16:1/20:3 | 18:0/20:4  | 18:1/20:4 | 18:1/20:5 | 18:2/22:6 |
|    | 16:0/20:4 | 10:0/22:0 | 16:1/20:4 | 18:0/20:5  | 18:1/22:4 | 18:1/20:4 | 20:1/20:4 |
|    | 16:0/22:4 | 10:1/10:1 | 16:1/22:4 | 18:0/22:4  | 18:1/22:0 | 18:1/22:4 | 20:1/22:5 |
|    | 10:0/22:5 | 10:1/10:1 | 10:1/22:5 | 10:0/22:5  | 10:1/10:1 |           |           |

**Supplementary Table 2** | Hydrocarbon chain profiles for PA, PC, PG, PI, PS, and PE. Red text represents an increased molecular abundance of the respective hydrocarbon chain profiles, while blue text represents a relative decrease molecular abundance the respective profiles between LPL KD vs control cells. Profiles that are listed more than one time represent fatty acyl groups that originate from a different position on the phospholipid backbone (e.g. sn1, sn2, sn3).



**Supplementary Figure 1** | AdipoRED<sup>TM</sup> staining of neutral lipid containing lipid droplets (LD)s in either Control or LPL KD primary microglia. (N=4 per group).



**Supplemental Figure 2** | (A-O) Gene expression in BV-2 microglial LPL KD vs control cells. (N=3 per group). (P-Q) Gene expression in primary microglial LPL KD vs control cells. (N=3 per group). \*P < 0.05. \*\*P < 0.01. \*\*\*P < 0.001.



**Supplemental Figure 3.** IDEP pathway analysis of relative gene expression differences in CD11b+ microglia isolated from 16 week old WT and MiLPLKD mice.



**Supplemental Figure 4.** Western blot analysis showing reduced LPL in primary mouse LPL KD microglia (**A**), and WT, 202 (shRNA control) and 553 (LPL KD) BV-2 microglia (previously shown in Bruce et al., 2018).