

Supplementary Materials:

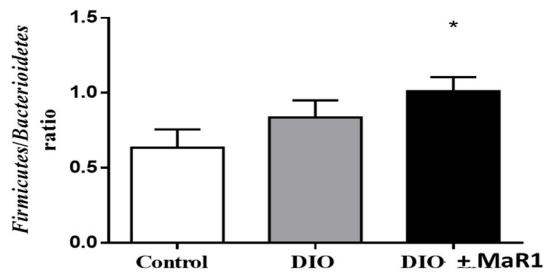


Figure S1. *Firmicutes/Bacteroidetes* ratio in Control and DIO mice treated by oral gavage with Maresin 1 (MaR1; 50 µg/kg/day) or treated with vehicle for 10 days. Data are expressed as mean ± SE (n=7-8). (□) Control; (▨) DIO; (■) DIO+ MaR1. *p<0.05 vs. Control.

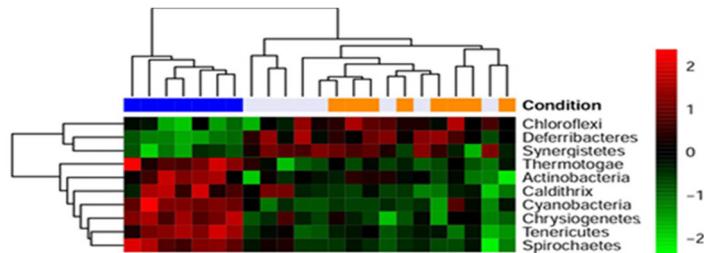


Figure S2. Heat map illustrating the relative abundance of the most different *Phyla* according to treatment group. (■) Control; (■) DIO; (▨) DIO+MaR1. In the heatmap, red and green indicate high and low abundance respectively relative to the mean abundance of all samples for each *Phyla*. DIO mice were treated by oral gavage with Maresin 1 (MaR1; 50 µg/kg/day) for 10 days.

Table S1. Taqman assays used for the gene expression analyses.

| Name | Gen | TaqMan probe |
|------------------------------------|--------------|---------------|
| Interleukin 6 | <i>Il-6</i> | Mm00446190_m1 |
| Interleukin 1 beta | <i>Il-1β</i> | Mm00434228_m1 |
| Monocyte chemoattractant protein 1 | <i>Mcp-1</i> | Mm00441242_m1 |
| Tumor Necrosis Factor alpha | <i>Tnf-α</i> | Mm00443258_m1 |
| 18S ribosomal RNA | <i>18S</i> | Mm03928990_g1 |

Table S2. Differential bacterial taxonomic profile at the *Phylum* level in DIO vs. Control and DIO+MaR1 vs. Control mice.

| Down-regulated DIO vs. Control | | | | Down-regulated DIO+MaR1 vs. Control | | | |
|--------------------------------|--------|--------|-----------------|-------------------------------------|--------|-----------------|--|
| <i>Phylum</i> | LogFC | p | adj. p Value | LogFC | p | adj. p Value | |
| <i>Tenericutes</i> | -3.316 | <0.001 | <0.001 | -3.542 | <0.001 | <0.001 | |
| <i>Caldithrix</i> | -2.358 | 0.001 | 0.003 | -1.894 | 0.005 | 0.011 | |
| <i>Spirochaetes</i> | -2.217 | <0.001 | <0.001 | -2.160 | <0.001 | <0.001 | |
| <i>Verrucomicrobia</i> | -1.862 | 0.050 | 0.087 | -2.468 | 0.011 | 0.022 | |
| <i>Chrysiogenetes</i> | -1.470 | <0.001 | <0.001 | -1.539 | <0.001 | <0.001 | |
| <i>Thermotogae</i> | -1.328 | <0.001 | <0.001 | -1.610 | <0.001 | <0.001 | |
| <i>Cyanobacteria</i> | -1.039 | <0.001 | <0.001 | -1.186 | <0.001 | <0.001 | |
| <i>Actinobacteria</i> | -0.770 | 0.002 | 0.005 | -0.743 | 0.003 | 0.007 | |

| Up-regulated DIO vs. Control | | | | Up-regulated DIO+ MaR1 vs. Control | | | |
|------------------------------|-------|--------|-----------------|------------------------------------|--------|-----------------|--|
| <i>Phylum</i> | LogFC | p | adj. p Value | LogFC | p | adj. p Value | |
| <i>Proteobacteria</i> | 0.225 | 0.334 | 0.467 | 0.480 | 0.046 | 0.065 | |
| <i>Firmicutes</i> | 0.385 | 0.106 | 0.171 | 0.556 | 0.023 | 0.037 | |
| <i>Chloroflexi</i> | 0.605 | 0.003 | 0.007 | 0.442 | 0.025 | 0.037 | |
| <i>Nitrospirae</i> | 0.671 | 0.040 | 0.077 | 0.745 | 0.024 | 0.037 | |
| <i>Synergistetes</i> | 0.935 | 0.005 | 0.011 | 1.667 | <0.001 | <0.001 | |
| <i>Defribacteres</i> | 3.508 | <0.001 | <0.001 | 3.809 | <0.001 | <0.001 | |

Negative Log Fold Change (LogFC) was related to lower representation in DIO or DIO+MaR1 compared to Control group, whereas positive LogFC corresponds to those *Phyla* that were increased in DIO or DIO+MaR1 compared with Control mice. *Phyla* were organized by their LogFC. DIO mice were treated by oral gavage with Maresin 1 (MaR1; 50 µg/kg/day) for 10 days.

Table S3. Differential bacterial taxonomic profile at the *Genus* level in DIO vs. Control mice.

| Down-regulated in DIO vs. Control | | | Up-regulated in DIO vs. Control | | |
|-----------------------------------|--------|-------------------------|---------------------------------|-------|--------|
| Genus | LogFC | p | Genus | LogFC | p |
| <i>Anaeroplasma</i> | -7.855 | 6.99 x10 ⁻¹¹ | <i>Caldilinea</i> | 0.484 | 0.043 |
| <i>Sutterella</i> | -7.764 | 2.98 x10 ⁻⁰⁹ | <i>Moraxella</i> | 0.641 | 0.033 |
| <i>Johnsonella</i> | -7.137 | 3.74 x10 ⁻¹⁷ | <i>Deferrribacter</i> | 0.724 | 0.023 |
| <i>Coprococcus</i> | -6.327 | 7.67 x10 ⁻⁰⁶ | <i>Methylobacterium</i> | 0.802 | 0.029 |
| <i>Allobaculum</i> | -6.151 | 2.27 x10 ⁻⁰⁶ | <i>Ehrlichia</i> | 0.819 | 0.032 |
| <i>Anaerostipes</i> | -6.067 | 6.59 x10 ⁻¹¹ | <i>Deinococcus</i> | 0.836 | 0.026 |
| <i>Limnobacter</i> | -5.800 | 3.63 x10 ⁻⁰⁸ | <i>Microcoleus</i> | 0.854 | 0.010 |
| <i>Desulfosarcina</i> | -5.609 | 2.62 x10 ⁻⁰⁸ | <i>Amoebophilus</i> | 0.889 | 0.005 |
| <i>Brachyspira</i> | -5.035 | 2.03 x10 ⁻¹¹ | <i>Paenibacillus</i> | 0.900 | 0.002 |
| <i>Bifidobacterium</i> | -4.636 | 2.78 x10 ⁻⁰⁹ | <i>Streptomyces</i> | 0.904 | 0.006 |
| <i>Turicibacter</i> | -4.396 | 6.05 x10 ⁻⁰⁴ | <i>Adlercreutzia</i> | 0.955 | 0.017 |
| <i>Geobacter</i> | -4.185 | 1.26 x10 ⁻⁰⁵ | <i>Dehalobacterium</i> | 0.969 | 0.029 |
| <i>Roseburia</i> | -3.873 | 5.55 x10 ⁻⁰⁴ | <i>Streptococcus</i> | 1.085 | 0.001 |
| <i>Novispirillum</i> | -3.805 | 3.41 x10 ⁻⁰³ | <i>Oscillospira</i> | 1.162 | 0.005 |
| <i>Sarcina</i> | -3.800 | 1.15 x10 ⁻⁰² | <i>Pseudomonas</i> | 1.183 | 0.013 |
| <i>Pseudobutyryrivibrio</i> | -3.653 | 1.31 x10 ⁻⁰³ | <i>Gluconobacter</i> | 1.260 | 0.038 |
| <i>Anaerovibrio</i> | -3.620 | 2.35 x10 ⁻⁰⁸ | <i>Enterobacter</i> | 1.429 | 0.035 |
| <i>Lachnolacterium</i> | -3.512 | 1.59 x10 ⁻⁰⁵ | <i>Flavobacterium</i> | 1.436 | 0.003 |
| <i>Dysgonomonas</i> | -3.418 | 3.94 x10 ⁻¹¹ | <i>Helicobacter</i> | 1.460 | <0.001 |
| <i>Prosthecobacter</i> | -3.377 | 2.45 x10 ⁻⁰² | <i>Desulfovibrio</i> | 1.476 | 0.001 |
| <i>Acholeplasma</i> | -3.171 | 1.25 x10 ⁻⁰⁴ | <i>Slackia</i> | 1.487 | 0.031 |
| <i>Mesoplasma</i> | -3.134 | 2.69 x10 ⁻⁰⁴ | <i>Kitasatospora</i> | 1.496 | 0.016 |
| <i>Luteolibacter</i> | -3.076 | 4.24 x10 ⁻⁰² | <i>Pedobacter</i> | 1.502 | <0.001 |
| <i>Legionella</i> | -3.049 | 2.62 x10 ⁻⁰⁹ | <i>Chromatium</i> | 1.520 | 0.002 |
| <i>Ulliginosibacterium</i> | -2.716 | 9.35 x10 ⁻⁰⁶ | <i>Alkaliphilus</i> | 1.717 | 0.000 |
| <i>Eggerthella</i> | -2.661 | 7.98 x10 ⁻⁰⁵ | <i>Thermobaculum</i> | 1.770 | 0.003 |
| <i>Eubacterium</i> | -2.638 | 6.29 x10 ⁻⁰⁵ | <i>Holdemania</i> | 1.787 | 0.005 |

Table S3 continuation

| Down-regulated in DIO vs. Control | | | Up-regulated in DIO vs. Control | | |
|-----------------------------------|--------|------------------------|---------------------------------|-------|--------|
| Genus | LogFC | p | Genus | LogFC | p |
| <i>Lysobacter</i> | -2.603 | 2.01 x10 ⁰² | <i>Ruminococcus</i> | 1.807 | <0.001 |
| <i>Caldithrix</i> | -2.444 | 6.28 x10 ⁰⁴ | <i>Capnocytophaga</i> | 1.860 | <0.001 |
| <i>Pectinatus</i> | -2.435 | 3.28x 10 ⁰⁵ | <i>Segetibacter</i> | 2.018 | <0.001 |
| <i>Marinitoga</i> | -2.371 | 4.30 x10 ⁰⁷ | <i>Rhodothermus</i> | 2.051 | <0.001 |
| <i>Desulfotomaculum</i> | -2.334 | 2.83 x10 ⁰⁴ | <i>Escherichia</i> | 2.068 | 0.029 |
| <i>Prevotella</i> | -2.331 | 1.17 x10 ⁰² | <i>Caldanaerobacter</i> | 2.069 | <0.001 |
| <i>Faecalibacterium</i> | -2.210 | 1.79 x10 ⁰⁴ | <i>Smithella</i> | 2.196 | <0.001 |
| <i>Parapedobacter</i> | -2.135 | 2.13 x10 ⁰⁵ | <i>Sphaerisporangium</i> | 2.218 | <0.001 |
| <i>Mannheimia</i> | -2.119 | 5.64 x10 ⁰⁴ | <i>Corynebacterium</i> | 2.274 | <0.001 |
| <i>Petrotoga</i> | -2.039 | 1.24 x10 ⁰³ | <i>Gluconacetobacter</i> | 2.283 | <0.001 |
| <i>Rhodospirillum</i> | -2.023 | 2.48 x10 ⁰² | <i>Lachnospira</i> | 2.303 | 0.001 |
| <i>Sedimentibacter</i> | -1.932 | 7.17 x10 ⁰⁶ | <i>Rikenella</i> | 2.325 | <0.001 |
| <i>Heliolestis</i> | -1.803 | 2.49 x10 ⁰⁵ | <i>Odoribacter</i> | 2.380 | <0.001 |
| <i>Muricauda</i> | -1.792 | 1.64 x10 ⁰⁶ | <i>Gillisia</i> | 2.478 | <0.001 |
| <i>Selenomonas</i> | -1.762 | 5.57 x10 ⁰⁴ | <i>Caloramator</i> | 2.616 | <0.001 |
| <i>Acinetobacter</i> | -1.565 | 1.92 x10 ⁰³ | <i>Vagococcus</i> | 3.060 | <0.001 |
| <i>Desulfurispirillum</i> | -1.556 | 1.63 x10 ⁰⁵ | <i>Acidaminobacter</i> | 3.127 | <0.001 |
| <i>Coraliomargarita</i> | -1.516 | 2.01 x10 ⁰² | <i>Peptococcus</i> | 3.289 | <0.001 |
| <i>Microbacterium</i> | -1.400 | 1.94 x10 ⁰³ | <i>Enterococcus</i> | 3.727 | <0.001 |
| <i>Butyrivibrio</i> | -1.357 | 4.22 x10 ⁰² | <i>Bilophila</i> | 3.758 | <0.001 |
| <i>Stenotrophomonas</i> | -1.282 | 1.77 x10 ⁰² | <i>Mucispirillum</i> | 3.793 | <0.001 |
| <i>Candidatus Phytoplasma</i> | -1.249 | 8.32 x10 ⁰⁴ | <i>Aquimarina</i> | 4.552 | <0.001 |
| <i>Butyricimonas</i> | -1.229 | 5.14 x10 ⁰³ | <i>Anaerotruncus</i> | 4.761 | <0.001 |
| <i>Emticicia</i> | -1.182 | 5.08 x10 ⁰³ | <i>Lactococcus</i> | 8.302 | <0.001 |
| <i>Caldicellulosiruptor</i> | -1.169 | 3.32 x10 ⁰³ | | | |
| <i>Luteibacter</i> | -1.165 | 2.26 x10 ⁰² | | | |
| <i>Kribbella</i> | -1.159 | 2.39 x10 ⁰² | | | |
| <i>Bradyrhizobium</i> | -1.151 | 1.09 x10 ⁰³ | | | |
| <i>Parabacteroides</i> | -1.125 | 3.97 x10 ⁰³ | | | |
| <i>Paraprevotella</i> | -0.982 | 3.58 x10 ⁰² | | | |
| <i>Dolichospermum</i> | -0.978 | 2.33 x10 ⁰² | | | |
| <i>Olivibacter</i> | -0.975 | 6.84 x10 ⁰⁴ | | | |
| <i>Marinobacter</i> | -0.917 | 2.95 x10 ⁰³ | | | |
| <i>Dyadobacter</i> | -0.877 | 8.02 x10 ⁰³ | | | |
| <i>Fervidobacterium</i> | -0.796 | 2.15 x10 ⁰² | | | |
| <i>Rhodobacter</i> | -0.786 | 3.47 x10 ⁰² | | | |
| <i>Thermus</i> | -0.742 | 7.25 x10 ⁰³ | | | |

Negative Log Fold Change (LogFC) was related to lower representation in DIO compared to Control whereas Positive LogFC corresponds to those *Genera* that were increased in DIO compared with Control. *Genera* were organized by their LogFC.