

**LncRNA *lncLy6C* induced by microbiota metabolite butyrate
promotes differentiation of Ly6C^{high} to Ly6C^{int/neg} macrophages
through *lncLy6C* /C/EBP β /Nr4A1 axis**

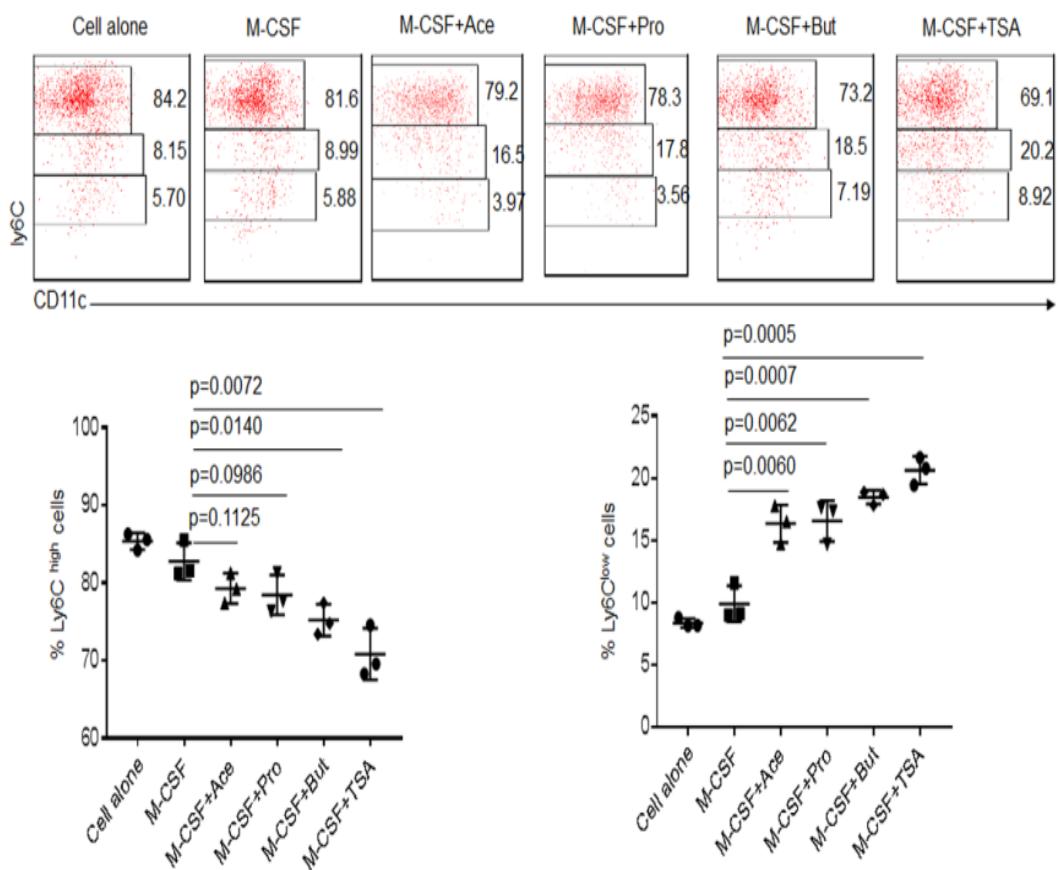


Fig. S1. Flow cytometry of CD117⁻CD11b⁺CD115⁺Ly6C⁺ BM monocytes after exposed to ascetic acid (Ace, 200 μ M), propionic acid (Pro, 200 μ M), butyrate (But, 200 μ M) and Trichostatin (TSA, 40 nM) for 2 days. % of Ly6C^{high} and Ly6C^{low} cells was compared (lower). Two side Student's *t*-test.

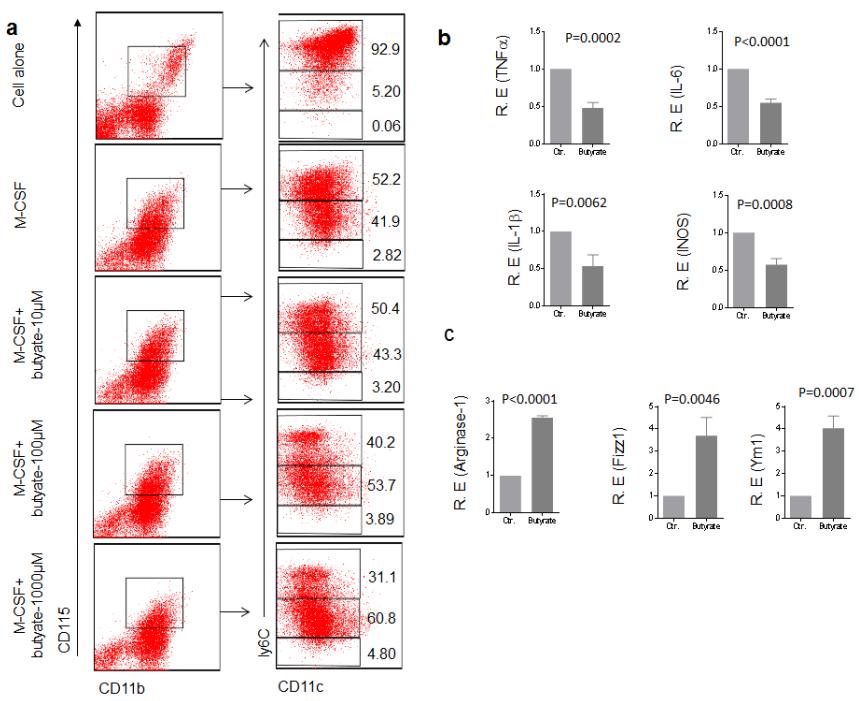


Fig. S2. Characteristics of CD117⁻ CD11b⁺ CD115⁺ Ly6C⁺ BM monocytes after

exposed to butyrate. a, Flow cytometry of CD117⁻ CD11b⁺ CD115⁺ Ly6C⁺ BM monocytes after exposed to different concentration (0, 10, 100 and 1000 μ M) of butyrate. **b,** QRT-PCR of TNF α , IL-6, IL-1 β and iNOS in CD117⁻ CD11b⁺ CD115⁺ Ly6C⁺ BM monocytes after exposed to butyrate (200 μ M). Ctrl., vehicle. **c,** QRT-PCR of arginase-1, Fizzi1 and Ym1 in CD117⁻ CD11b⁺ CD115⁺ Ly6C⁺ BM monocytes after exposed to butyrate (200 μ M). Ctrl., vehicle. Two side Student's *t*-test in b and c.

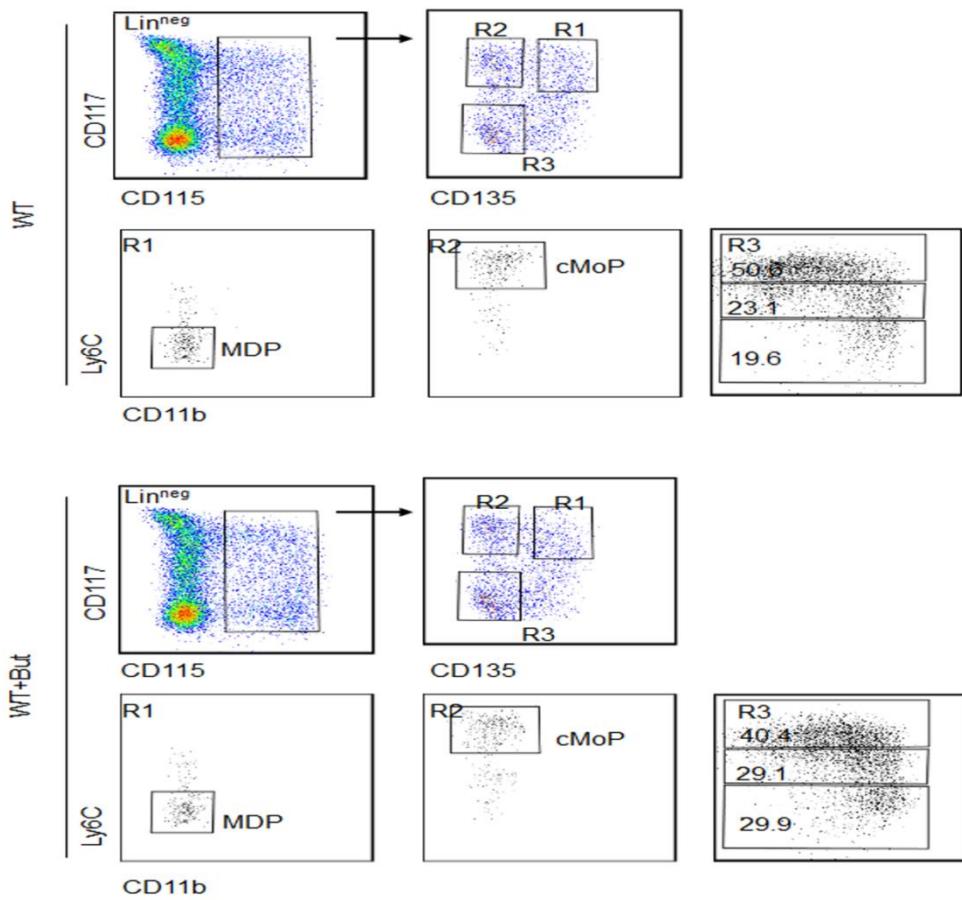


Fig. S3. Flow cytometry of bone marrow cells in wild type mice with (WT+But) or without (WT) butyrate. Mice received sodium butyrate (150 mM) in the drinking water for one week (n=5). One representative of 5 mice.

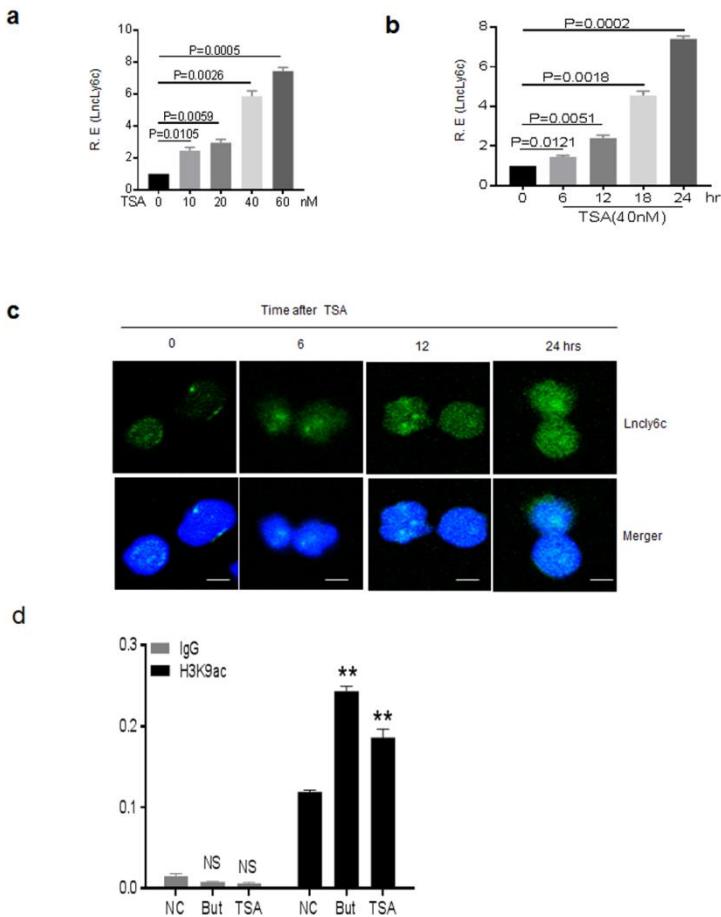


Fig. S4. Trichostatin induces the expression of *lncLy6C*. **a**, QRT-PCR of *lncLy6C* in BMDMs after exposed to different concentrations of Trichostatin A. R. E, relative expression. **b**, QRT-PCR of *lncLy6C* in BMDMs after exposed to Trichostatin A at different time points. R.E, relative expression. **c**, FISH of *lncLy6C* in BMDMs after exposed to Trichostatin A at different time points. Nuclei were stained with DAPI (blue); Green, *lncLy6C*. Scale bar, 2.5 μ M. **d**, Chip analyses in BMDMs after exposed to butyrate (200 μ M) or TSA (40nM, TSA) for 3 h. Samples were analyzed by ChIP using anti-H3K9Ac. Purified DNA was analyzed by qPCR using primers specific to the promoters of *lncLy6C*. IgG, isotypic antibody. % input was compared. ONE-way ANOVA and Bonferroni's Multiple Comparison Test in a and b. Two side Student's *t*-test in d.

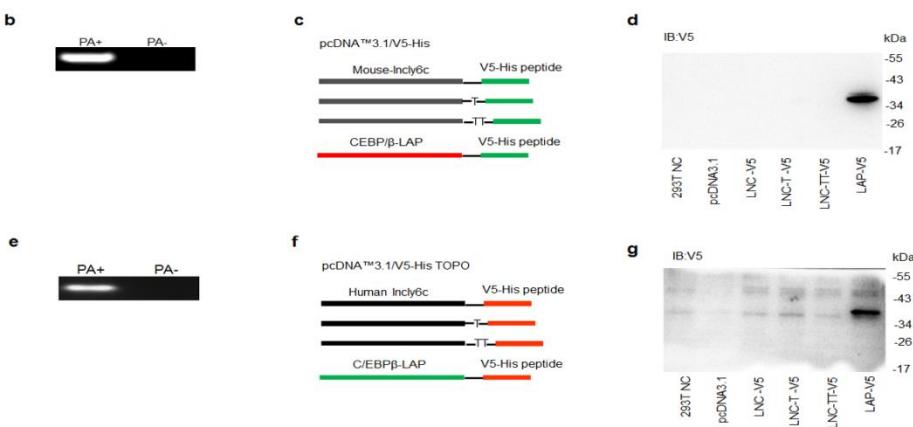
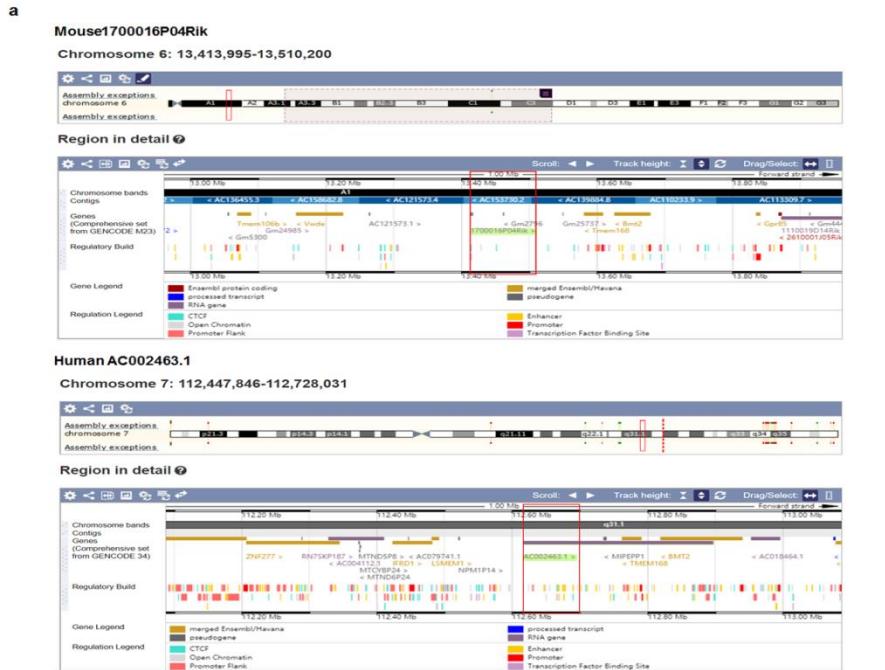


Fig. S5. Characteristics of *LncLy6C*. **a**, Location of mouse 1700016p04Rik (*lncLy6C*) and human AC0024631 (*Hu lncLy6C*). **b**, RT-PCR assay of mouse *lncLy6C* with polyA+ RNA. The polyA+ RNA fraction of mouse *lncLy6C* was examined using primer with poly-A (PA+) or primers without polyA (PA-). **c** and **d**, Immunoblotting of V5-tagged mouse *lncLy6C* transfected BMDMs. Full-length *lncLy6C* was cloned into pcDNA3.1 with N-terminal start codon ATG and C-terminal V5 tag in all three coding patterns (c) , and then these plasmids subsequently were transfected into HEK293T cells separately, and after 48 hours, immunoblotting was used to detect the flag-tagged protein (d). C/EBP β -LAP with V5 tag, a positive control (d). **e**, RT-PCR assay of hulncLy6C with polyA+ RNA. The polyA+ RNA fraction of hulncly6c was examined using primer with poly-A(PA+) or primers without polyA (PA-). **f** and **g**, Immunoblotting of V5-tagged human *HulncLy6C* transfected BMDMs. Full-length Hu-*lncly6c* was cloned into pcDNA3.1 with N-terminal start codon ATG and C-terminal V5 tag in all three coding patterns (f) , and then these plasmids subsequently were transfected into HEK293T cells

separately, and after 48 hours, immunoblotting was performed using anti -flag antibody (g). C/EBP β LAP with V5 tag, a positive control. No lncRNA encoding bands (around 20 kd) were found.

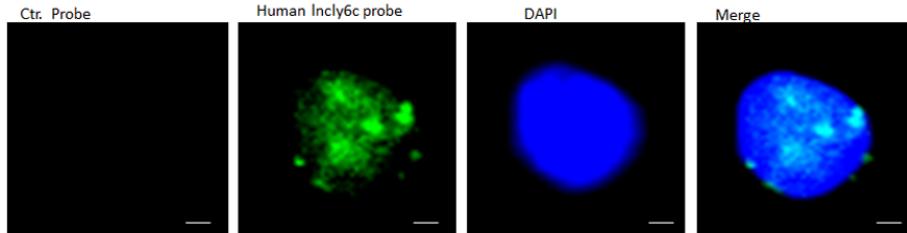
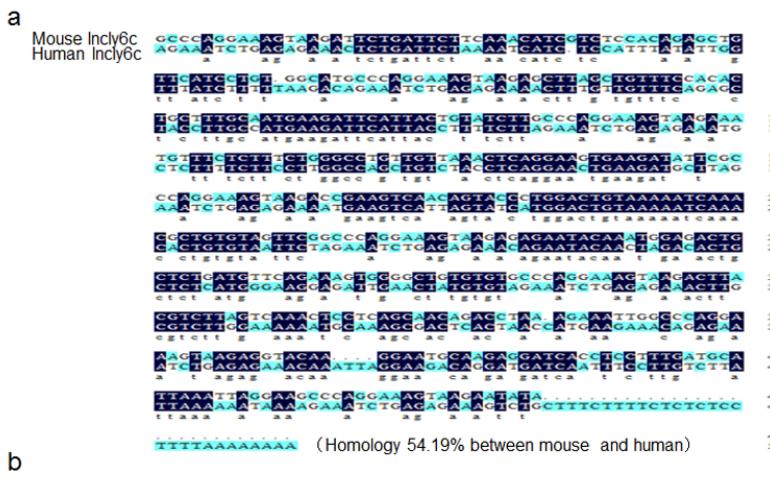


Fig. S6. Homology of human *lncLy6C* with mouse *lncLy6C*.

a, Homology analyses between mouse *lncLy6C* and human *lncLy6C*. Higher homology (54.19%) between mouse *lncLy6C* and human *hulncLy6C* was shown.

b, FISH of *hulncly6c* in CD14⁺ human peripheral blood cells. Green, human lncly6c; Blue, DAPI; Scale bar, 2.5 μM.

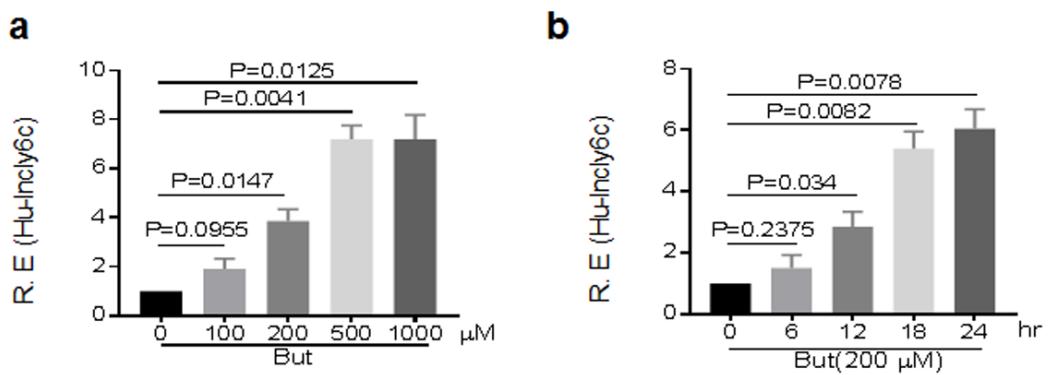


Fig. S7. Expression of *lncLy6C* in human CD14+ monocytes after exposed to butyrate. a QRT-PCR of *lncLy6C* in human CD14+ monocytes after exposed to different concentration of butyrate. R. E, relative expression. **b** QRT-PCR of *lncLy6C* in human CD14+ monocytes after exposed to butyrate (200 μ M) at different time points. R. E, relative expression. Two side Student's *t*-test.

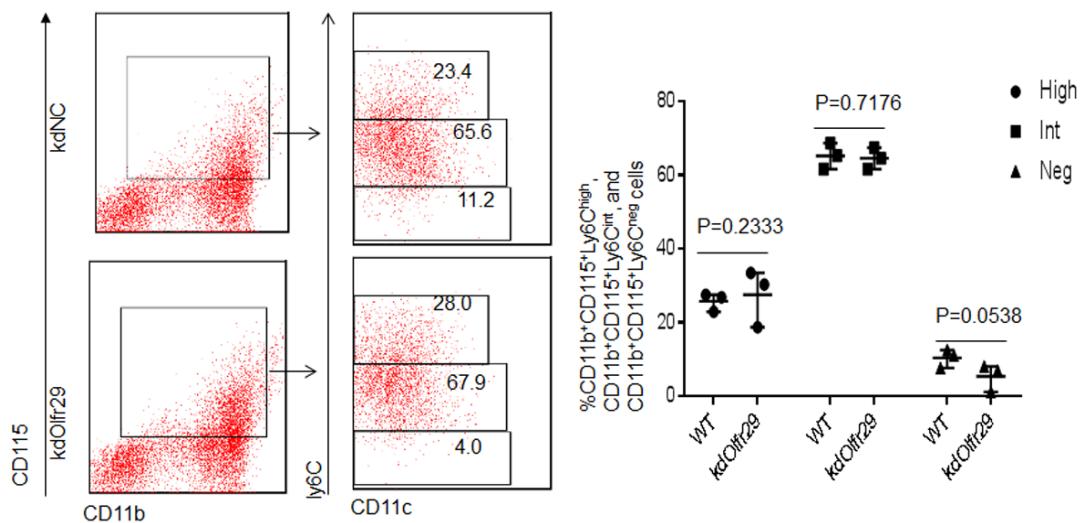


Fig. S8. Flow cytometry of $CD11b^+ CD115^+ Ly6C^{high}$, $CD11b^+ CD115^+ Ly6C^{int}$, $CD11b^+ CD115^+ Ly6C^{neg}$ cells in mouse BMC after silencing Olfr29-PS1 (kd Olfr29-PS1). Mouse BMCs were transfected by Olfr29-PS1 siRNA and then cultured for 4 days. KdNC, siRNA control. Two side Student's *t*-test.

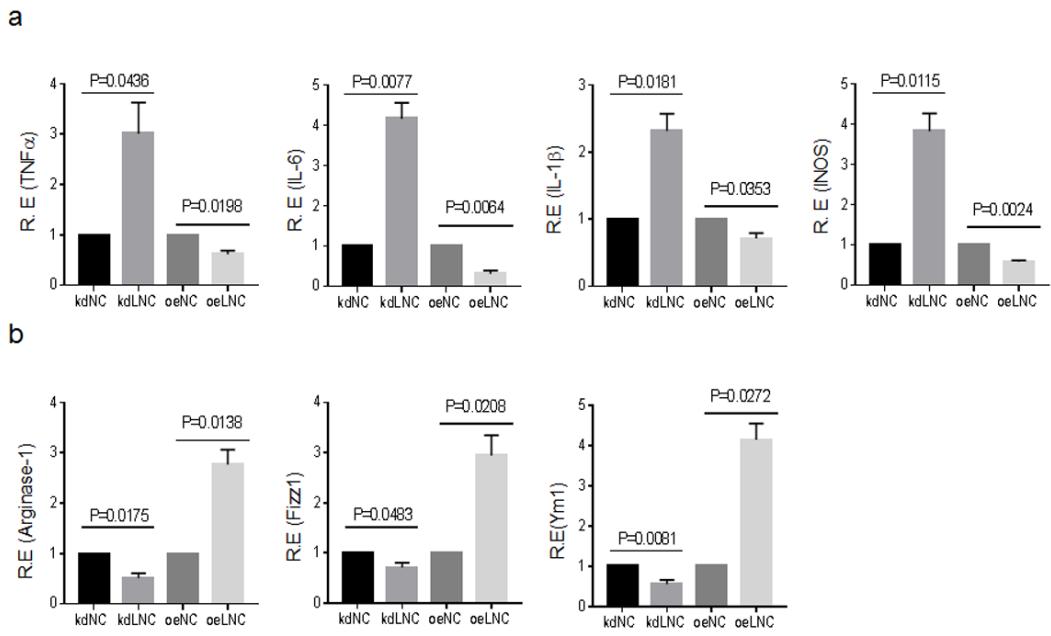


Fig. S9. LncLy6c affects the expression of cytokines, iNOS, Arginase-1, Fizz1 and Ym1. **a** QRT-PCR of TNF α , IL-6, IL-1 β and iNOS in CD117- CD11b+ CD115+ Ly6C+ BM monocytes after silencing LncLy6c or transfecting LncLy6c lentiviruses. **b** QRT-PCR of arginase-1, Fizz1 and Ym1 in CD117- CD11b+ CD115+ Ly6C+ BM monocytes after silencing LncLy6c or transfecting LncLy6c lentiviruses. kdNC, siRNA control; kdLNC, lncRNA siRNA; OcNC, empty lentivirus; OeLNC, lncRNA lentivirus. Two side Student's *t*-test.

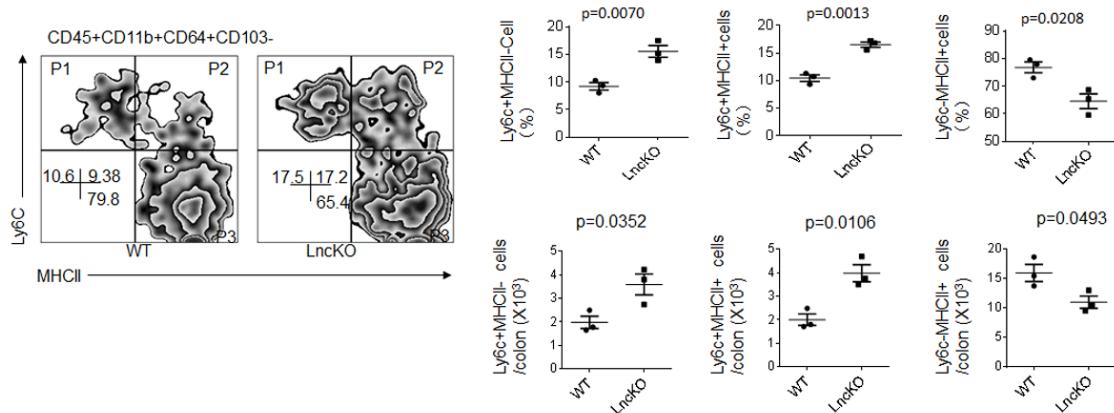


Fig. S10. Flow cytometry of MHCII⁺ Ly6C⁺ inflammatory macrophages.

CD45⁺ CD11b⁺ CD64⁺ CD103⁻ MHCII⁺ Ly6C⁺ cells in the colonic tissues of WT or Lncly6c KO mice (n = 6). % cells and total Ly6c⁺ MHCII⁺ cell number per colon were analyzed (right). Two side Student's *t*-test.

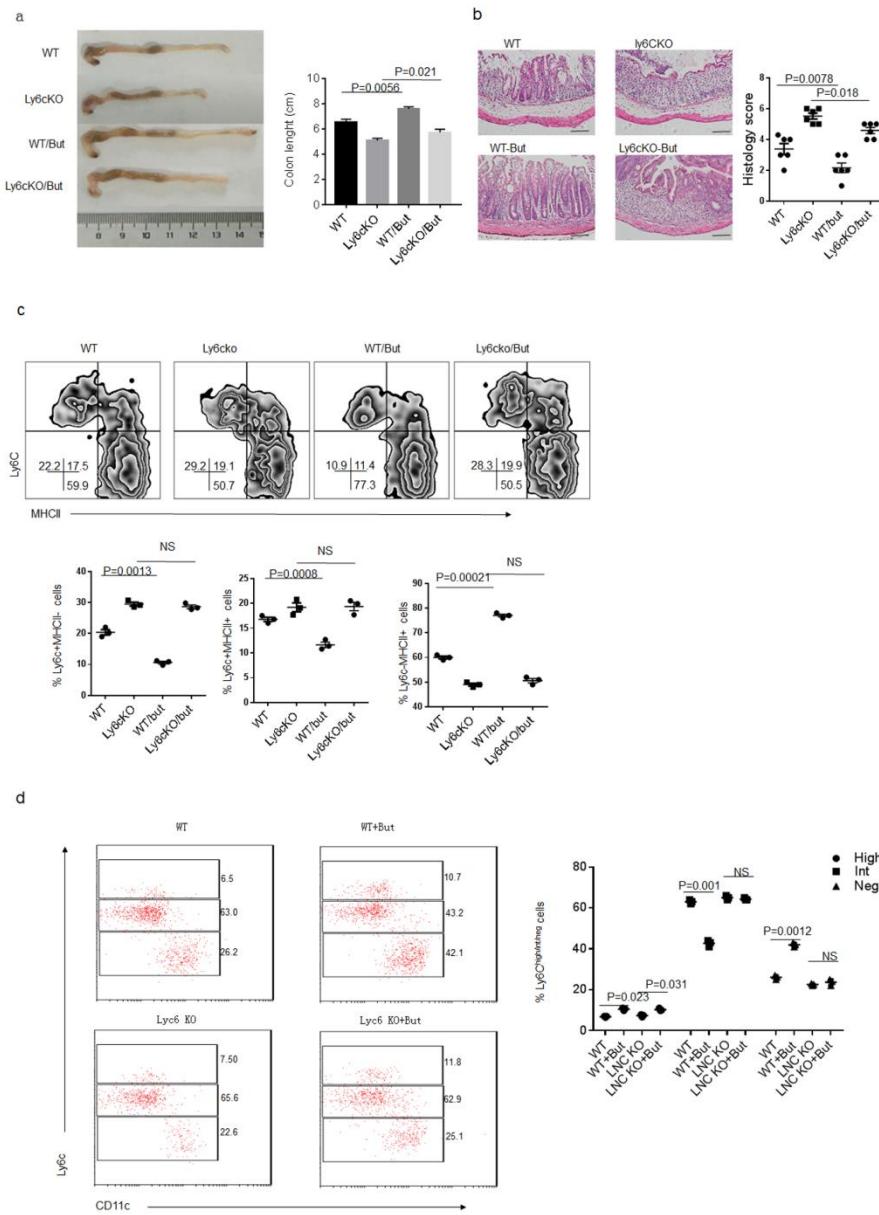


Fig. S11. Butyrate promotes differentiation of Ly6c^{high} inflammatory macrophages into Ly6c^{negative} macrophages in DSS-treated WT but not *LncLy6c* KO mice. **a** The length of colon in LncLy6c KO and WT mice with or without butyrate after DSS (2.5%) treatment (n=6). **b** H&E staining and histology score of colon tissues in LncLy6c KO and WT mice with or without butyrate after DSS (2.5%) treatment. For histological score, 3 slides/mouse, n=6. Scale bar, 40 μ M. **c** Flow cytometry of CD45⁺CD11b⁺CD64⁺CD103⁺MHC⁺Ly6C⁺ in colon tissues in Lynly6c KO and WT mice with or without butyrate after DSS (2.5%) treatment (n=3).

d Flow cytometry of CD11b⁺CD115⁺Ly6C^{high}, CD11b⁺CD115⁺Ly6C^{int}, CD11b⁺CD115⁺Ly6C^{neg} cells in lncLy6c KO and WT mice with or without butyrate after DSS (2.5%) treatment (n=3). Two side student's *t*-test; NS, no significance.

Supplementary Table S1. Immunoprecipitation in BMDMs using anti-C/EBP β antibody.

| Description | Σ Coverage | Score C/EBP β Ab | Coverage C/EBP β Ab | Score Isotypic Ab | Coverage Isotypic Ab | MW [kDa] | calc. pl |
|---------------|-------------------|---------------------------|------------------------------|----------------------|-------------------------|-------------|-------------|
| C/EBP β | 17.93 | 8.85 | 17.93 | 0 | 0 | 15.6 | 9.95 |
| ASH2L | 2.43 | 2.43 | 2.43 | 0 | 0 | 60.1 | 6.95 |
| WDR5 | 17.07 | 10.32 | 17.07 | 0 | 0 | 36.6 | 8.27 |
| RNF2 | 2.68 | 2.68 | 2.68 | 0 | 0 | 37.6 | 6.84 |
| CXXC1 | 15.61 | 22.72 | 11.06 | 7 | 8 | 76.1 | 8.27 |

Supplementary Table S2. Reagents and oligoes used in this study.

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|--|---------------------------|--------------------------------|
| Antibodies | | |
| β-Actin Antibody | Santa Cruz | Cat:sc-47778 RRID:AB_626632 |
| Anti-C/EB β Antibody | Abcam | Cat:ab15050 RRID:AB_301598 |
| V5 Tag Monoclonal Antibody | Thermo Fisher Scientific | Cat:MA5-15253 RRID:AB_10977225 |
| Anti-Histone H3 (tri methyl K4) antibody | Abcam | Cat:ab8580 RRID:AB_306649 |
| WDR5 Rabbit mAb | Cell Signaling Technology | Cat:13105 RRID:AB_2620133 |
| Anti-Nr4a1 Antibody | Abcam | Cat:ab13851 RRID:AB_300679 |
| Anti-N6-methyladenosine (m6A) antibody | Abcam | Cat:ab208577 RRID:AB_2753144 |
| Anti-METTL3 antibody | Abcam | Cat:ab195352 RRID:AB_2721254 |
| Anti-STAT3 (phospho Y705) antibody | Abcam | Cat:ab76315 RRID:AB_1658549 |
| Anti-ASH2L antibody | Abcam | Cat:ab50699 RRID:AB_867739 |
| Anti-RbBP5 antibody | Abcam | Cat:ab52084 RRID:AB_882299 |
| Anti-DPY30 antibody | Abcam | Cat:ab126352 RRID:AB_11128034 |
| Anti-MLL1 (D2M7U) Rabbit antibody | Cell Signaling Technology | Cat:14689 RRID:AB_2688009 |
| Rabbit Anti-CD11c antibody | Bioss Inc | Cat: bs-2508R RRID:AB_10855986 |
| Rabbit Anti-CD4 antibody | Bioss Inc | Cat: bs-0766R RRID:AB_10857931 |
| Rabbit Anti-CD8 antibody | Bioss Inc | Cat: bs-0648R RRID:AB_10857537 |
| Rabbit Anti-CD19 antibody | Bioss Inc | Cat: bs-0079R RRID:AB_10857264 |
| Rat Anti-Ly6C Monoclonal antibody | Novus | Cat:NB100-65414 RRID:AB_964346 |
| F4/80 (6A545) antibody | Santa Cruz | Cat:sc-71085 RRID:AB_1122717 |
| APC anti-mouse CD45.2 Antibody | Biolegend | Cat: 109814 RRID:AB_389211 |
| APC anti-mouse CD11c Antibody | Biolegend | Cat: 117310 RRID:AB_313779 |
| APC anti-mouse CD117 (c-Kit) Antibody | Biolegend | Cat: 105812 RRID:AB_313221 |
| APC/Cy7 anti-mouse/human CD11b Antibody | Biolegend | Cat: 101226 RRID:AB_830642 |
| PerCP anti-mouse/human CD11b Antibody | Biolegend | Cat: 135506 RRID:AB_1937253 |
| FITC anti-mouse CD11c Antibody | Biolegend | Cat: 117306 RRID:AB_313775 |
| FITC anti-mouse Ly-6C Antibody | Biolegend | Cat: 128006 RRID:AB_1186135 |
| FITC anti-mouse CD3 Antibody | Biolegend | Cat: 100204 RRID:AB_312661 |
| FITC anti-mouse CD19 Antibody | Biolegend | Cat: 152404 RRID:AB_2629813 |
| FITC anti-mouse Gr-1 Antibody | Biolegend | Cat: 108406 RRID:AB_313371 |
| PE anti-mouse CD115 (CSF-1R) Antibody | Biolegend | Cat: 135506 RRID:AB_1937253 |
| PE/Cy5 anti-mouse CD135 Antibody | Biolegend | Cat: 135312 RRID:AB_2263031 |
| PE/Cy7 anti-mouse Ly-6C Antibody | Biolegend | Cat: 128017 RRID:AB_1732093 |
| Bacterial and Virus Strains | | |

| | | |
|---|--------------------------|--|
| BL21 Chemically Competent cell | TransGen Biotech | Cat:CD901-01 |
| DH5 α Chemically Competent cell | Tiangen Biotech | Cat:CD101-03 |
| Chemicals, Peptides, and Recombinant Proteins | | |
| Recombinant Murine GM-CSF | PeproTech | Cat:315-03 |
| Recombinant Murine M-CSF | PeproTech | Cat:315-02 |
| HiPerFect Transfection Reagent | QIAGEN | Cat:301705 |
| Trichostatin A | MCE | Cat: HY-15144 |
| Pertussis Toxin | MCE | Cat: HY-112779 |
| Polybrene | Millipore | Cat:sc-134220 |
| Lipofectamine™ 3000 Transfection Reagent | Thermo Fisher Scientific | Cat:11668027 |
| Trizol | Life technologies | Cat:15596018 |
| Oligonucleotides for clone genes | | |
| Murine LncLy6C FW | BGI | 5'-GGTCGGAGTGGATGGCCC -3' |
| Murine LncLy6C REV | BGI | 5'-TATATTCCTAATTAATGCATCAAAGG -3' |
| Human LncLy6C FW | BGI | 5'-GGAGTTGGCTGCCAGAAATC-3' |
| Human LncLy6C REV | BGI | 5'-TAAAAGGAGAGAGAAAAGAAAGCAG-3' |
| Murine LncLy6C-L1 FW | BGI | 5'-GGATGGCCCAGGAAAGTAAGAC-3' |
| Murine LncLy6C-L2 FW | BGI | 5'-GTAAAATCAAACGCTGTGTAG-3' |
| Murine LncLy6C-L3 FW | BGI | 5'-GTGTGTCTTACGTCTTAGTC-3' |
| Murine LncLy6C-L4 FW | BGI | 5'-ACAAGGAATGCAAGAGGATC-3' |
| Murine LncLy6C-MUT1 FW | BGI | 5'-CGAAGTCAACAGTACCCGGCTGTAAAAATCAAACGCTGTG-3' |
| Murine LncLy6C-MUT1 REV | BGI | 5'-CACAGCGTTGATTTTACAGCCCAGGGTACTGTGACTTCG-3' |
| Murine LncLy6C-MUT2 FW | BGI | 5'-CGAAGTCAACAGTACCCGGCTGTAAAAATCAAACGCTGTG-3' |
| Murine LncLy6C-MUT2 REV | BGI | 5'-CACAGCGTTGATTTTACAGACCAGGGTACTGTGACTTCG-3' |
| Murine LncLy6C-MUT3 FW | BGI | 5'-CGAAGTCAACAGTACCCGGCTGTAAAAATCAAACGCTGTG-3' |
| Murine LncLy6C-MUT3 REV | BGI | 5'-CACAGCGTTGATTTTACAGCCCAGGGTACTGTGACTTCG-3' |
| Murine LncLy6C-MUT4 FW | BGI | 5'-AGTCGGAGAACAAATGGGGACTGCTCTGATGTTCAGAAAG-3' |
| Murine LncLy6C-MUT4 REV | BGI | 5'-CTTCTGAACATCAGAGCAGTCCCCATTGTATTCTCCGAAC-3' |
| Murine LAP* FW | BGI | 5'-GCCACCATGCACCGCCTGCTGGCCTGGACG-3' |
| Murine LAP* REV | BGI | 5'-GCAGTGGCCCGCCGAGGCCA-3' |

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|------------------------------|-----|--|
| Murine LAP FW | BGI | 5'-GCCACCATGGAAGTGGCCAACCTTACTACGAG C-3' |
| Murine LAP REV | BGI | 5'-GCAGTGGCCCGCCGAGGCCA-3' |
| Murine LIP FW | BGI | 5'-GCCACCATGGCGGCCGGTTCCCCTTCG-3' |
| Murine LIP REV | BGI | 5'-GCAGTGGCCCGCCGAGGCCA-3' |
| Murine Δ LAP* FW | BGI | 5'-GCCACCATGCACCGCCTGCTGGCCTGGACG-3' |
| Murine Δ LAP* REV | BGI | 5'-GGCGGGCGCGTCGTCCCGCGCTTG-3' |
| Murine Δ LAP FW | BGI | 5'-GCCACCATGGAAGTGGCCAACCTTACTACGAG C-3' |
| Murine Δ LAP REV | BGI | 5'-GGCGGGCGCGTCGTCCCGCGCTTG-3' |
| Murine WDR5 FW | BGI | 5'-GCCACCATGGCACAGAGGAGAAAGAAGC-3' |
| Murine WDR5 REV | BGI | 5'-GCAGTCACTCTTCCACAGTTGATT-3' |
| Murine ASH2L FW | BGI | 5'-GCCACCATGGCGGCCGCTGGAGCGGGT -3' |
| Murine ASH2L REV | BGI | 5'-GGGTTCCCAGGGTGGACTACGTCTT-3' |
| Murine DPY30 FW | BGI | 5'-GCCACCATGGAGTCGGAGCAGATGCTGGAGG-3' |
| Murine DPY30 REV | BGI | 5'-ATTCGATCTCAAAC TGCGCCTG-3' |
| Murine RBBP5 FW | BGI | 5'-GCCACCATGAACCTCGAGTTGCTGGAGTCCT-3' |
| Murine RBBP5 REV | BGI | 5'-CAGCAGTTCTGAGATGGCTCCTCCT-3' |
| Oligonucleotides for qRT-PCR | | |
| Murine GAPDH FW | BGI | 5'-TCAACGGCACAGTCAGG-3' |
| Murine GAPDH REV | BGI | 5'-TACTCAGCACCGGCCTCA-3' |
| Murine Arg1 FW | BGI | 5'- CTGACCTATGTGTCATTGGG -3' |
| Murine Arg1 REV | BGI | 5'- TCAGGAGAAAGGACACAGGTT -3' |
| Murine INOS FW | BGI | 5'-CTTGGAGCGAGTTGTGGATTGT-3' |
| Murine INOS REV | BGI | 5'-AGGTGAGGGCTTGGCTGAGTGA-3' |
| Murine TNFa FW | BGI | 5'-CCAGACCCTCACACTCAGATCA-3' |
| Murine TNFa Rev | BGI | 5'-GTAGACAAGGTACAACCCATCG-3' |
| Murine IL-1b FW | BGI | 5'-GCAGGCAGTATCACTCATTGTG-3' |
| Murine IL-1b Rev | BGI | 5'-AGGCTTTTTGTTGTTCATCTC-3' |
| Murine IL-6 FW | BGI | 5'-ACAACCACGGCCTTCCCTACTT-3' |
| Murine IL-6 Rev | BGI | 5'-TTTCTCATTTCCACGATTCCC-3' |
| Murine FiZZ1 FW | BGI | 5'-AGACTACAAC TTGTTCCCT-3' |
| Murine FiZZ1 Rev | BGI | 5'-GTTCTTGACCTTATTCTCCAC-3' |
| Murine YM-1 Fw | BGI | 5'-CGTAATCAAGTCTGGTACAAG-3' |
| Murine YM-1 Rev | BGI | 5'-AGGGTCACTCAGGATAAAAGGTA-3' |
| Murine Nr4A1 Fw | BGI | 5'-TGAGTTCGGAAGCCTACCAT-3' |
| Murine Nr4A1 Rev | BGI | 5'-GGAGGAGGCAGAGGAACAAGC-3' |
| Murine LncLy6C FW | BGI | 5'-CCCAGGAAAGTAAGACCA-3' |
| Murine LncLy6C REV | BGI | 5'-TTAACACAGGCCAGA-3' |
| Human Lncly6C FW | BGI | 5'- AGACATGAAAGTCTGCTCACC-3' |
| Human Lncly6C REV | BGI | 5'- CTTCATAAGCATCTTCAGTTCT-3' |
| Murine Gm8883 FW | BGI | 5'-GTCTGTGTGCTAGCTCT-3' |
| Murine Gm8883 REV | BGI | 5'-CTGCTCTGGAAC TCACTCTGTA-3' |
| Murine 5730403I07Rik FW | BGI | 5'- AAGGGAAC TCA CGGTGGT -3' |

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|--|-----|---|
| Murine 5730403I07Rik REV | BGI | 5'- TGATGTTTCAGCGAGGGA-3' |
| Murine Efcab8 FW | BGI | 5'-TGTGCCTACTGCTCTTCTCCC-3' |
| Murine Efcab8 REV | BGI | 5'-TGCCCTCTCAAACACCTTC-3' |
| Murine Meg3 FW | BGI | 5'-TTGAAATAAAGGAGTGACAGAA -3' |
| Murine Meg3 REV | BGI | 5'-CCCAGAATAAGATGAGCAGAAG-3' |
| Murine Olfr29-ps1 FW | BGI | 5'-GACATCTGCTACACCACCTCCT-3' |
| Murine Olfr29-ps1 REV | BGI | 5'-CGATCAAACGCCATCATCTCA-3' |
| Murine 4930528A17Rik FW | BGI | 5'-AGTTCTGGAAGCAGGGTGTGTTG-3' |
| Murine 4930528A17Rik REV | BGI | 5'-CTTTTACCTCTTCGGGAGGC-3' |
| Murine BC021767 FW | BGI | 5'-AGCAGGGAGGGAACATTATGGG -3' |
| Murine BC021767 REV | BGI | 5'-TGAGAGTAAAGCAGCAAGGCAG -3' |
| Murine 1500009C09Rik FW | BGI | 5'-TTCTGTTCCCATCTGTGTTGC-3' |
| Murine 1500009C09Rik REV | BGI | 5'-GGTGAGCGGGCTGATCTATA-3' |
| Murine Gm5468 FW | BGI | 5'-TTGCTTGTTCTGCTCGTCCT-3' |
| Murine Gm5468 REV | BGI | 5'-CCTTGGCATTCTCGTCTCCCTA-3' |
| Murine Gm5105 FW | BGI | 5'-CAGAGAGCGTGGTAGAGGATT-3' |
| Murine Gm5105 REV | BGI | 5'-GGAAGAGACAAAGGGGGACAT-3' |
| Murine Speer5-ps1 FW | BGI | 5'-ACAAGCAAGAACAGTTGAG-3' |
| Murine Speer5-ps1 REV | BGI | 5'-GCTGGGCAGGTTACGATAGAA-3' |
| Oligonucleotides used in 5'- and 3'-RACE | | |
| Murine LncLy6C 5'RACE | BGI | 5'-CAATTCTTCTGGCTGTTGCT -3' |
| Murine LncLy6C 3'RACE | BGI | 5'-ATCTTAATGTTCTCTTCTGG -3' |
| UPM long primer for 5'RACE | BGI | 5'-TAATACGACTCACTATAGGGCAAGCAGTGGTAT CAACGCAGAGT-3' |
| UPM short primer for 5'RACE | BGI | 5'-CTAATACGACTCACTATAGGGC-3' |
| Oligonucleotides used in CHIP-PCR | | |
| Nr4A1-H3K4me3 FW for CHIP-PCR | BGI | 5'-CCTCCTCCTGGCCGCCTCCC-3' |
| Nr4A1-H3K4me3 REV for CHIP-PCR | BGI | 5'-AGCACACTCCCCAACCTTC-3' |
| Lncly6C-H3K9ac FW for CHIP-PCR | BGI | 5'-GCCAGGAAAGTAAGACCATAGC-3' |
| Lncly6C-H3K9ac REV for CHIP-PCR | BGI | 5'-ACAACAGGCCAGAAAGAGAAC-3' |
| C/EBP β FW for CHIP-PCR | BGI | 5'- TCCACAAACAGAAAGCCTACCT -3' |
| C/EBP β REV for CHIP-PCR | BGI | 5'- ACCTTCCCAGTGTCAACCCAAT -3' |
| Oligonucleotides used in Northern blot | | |
| T7- Murine LncLy6C -FW | BGI | 5'- CTGATTCTCAAACATCGTCTC-3' |
| T7- Murine LncLy6C-REV | BGI | 5'- TAATACGACTCACTATAGGGCATTCTGTACCAA TTTCTT -3' |
| T7-U6 RNA-FW | BGI | 5'-GTGCTCGCTCGGCAGCACATATAC-3' |
| T7-U6 RNA-REV | BGI | 5'-TAATACGACTCACTATAGGGAAAAATATGGAAC GCTTCACGAATT-3' |
| Probes used in the RNA-FISH | | |
| Murine LncLy6C-FAM | BGI | 5'-FAM-AAGCATCTTCAGTCCCTGAGGTAGA -3' |
| Human LncLy6C-FAM | BGI | 5'- FAM-ATTTTTCCAAGACGCAAGACACAT-3' |

| | | |
|--|--------------------------|-------------------------------------|
| NC-FAM | BGI | 5'-FAM--CGGGAGCCTAGGAAGTGCATTTTC-3' |
| siRNAs used in this study | | |
| Murine LncLy6C | Ribobio | 5'-CCTCAGCAACAGACCTAAA-3' |
| Mettl3 siRNA-1 | Ribobio | 5'-GCTACCGTATGGGACATTA -3' |
| Mettl3 siRNA-2 | Ribobio | 5'-CCGCAAGATTGAGTTATT -3' |
| Other | | |
| pcDNA™3.1/V5-His TOPO® TA Expression Kit | Invitrogen | Cat: K4800-40 |
| Pierce™ Magnetic RNA-Protein Pull-Down Kit | Thermo Fisher Scientific | Cat:20164 |
| Dual-Luciferase® Reporter Assay System | Promega | Cat: E1960 |
| DIG Northern Starter Kit | Roche | Cat:12039672910 |
| Pierce™ Protein G Agarose | Thermo Fisher Scientific | Cat: 20397 |
| FirstChoice RLM-RACE Kit | Ambion | Cat: AM1700 |
| EZ-ChIP™Chromatin Immunoprecipitation Kit | Millipore | Cat:17-371 |