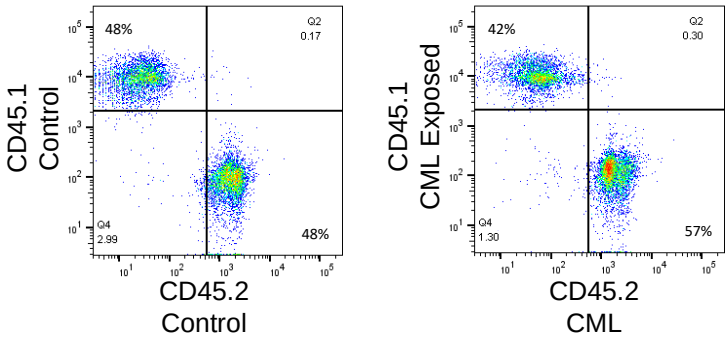
Supplemental Fig. S1

a



b

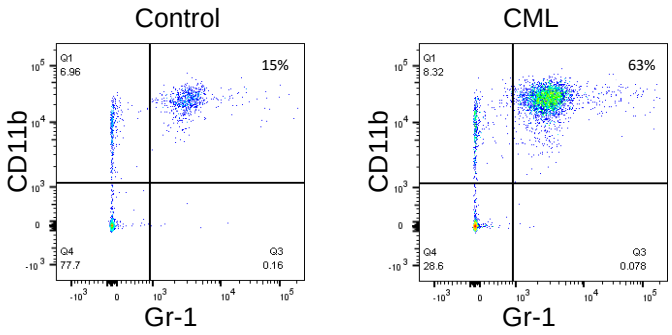
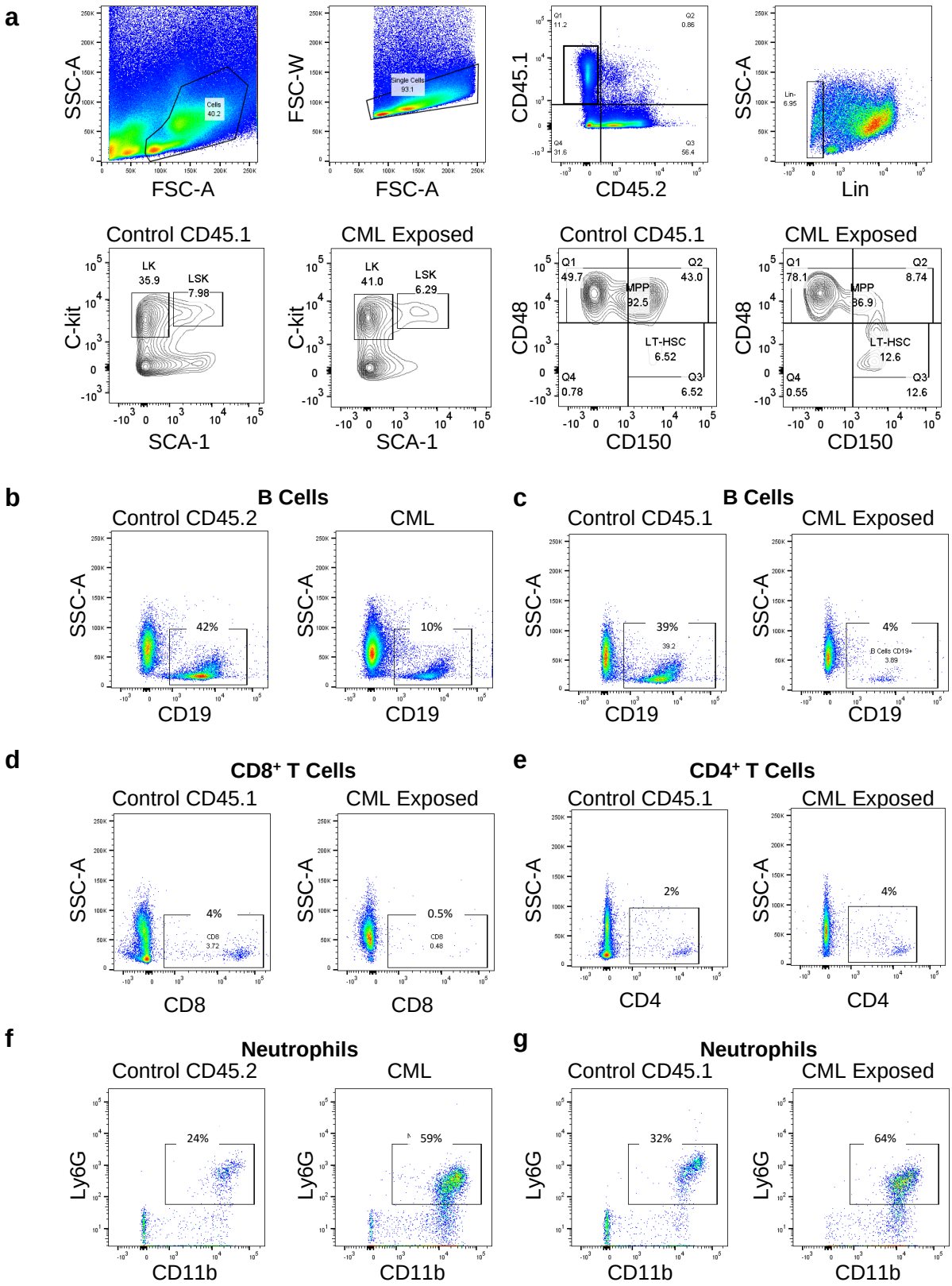


Fig. S1: Flow cytometry analysis of bone marrow (BM) of chimeric mice after BCR-ABL induction. **a:** Representative flow cytometry plot of chimerism in BM. **b:** Representative flow cytometry plots of myeloproliferation in BM.

Supplemental Fig. S2



Supplemental Fig. S2 cont.

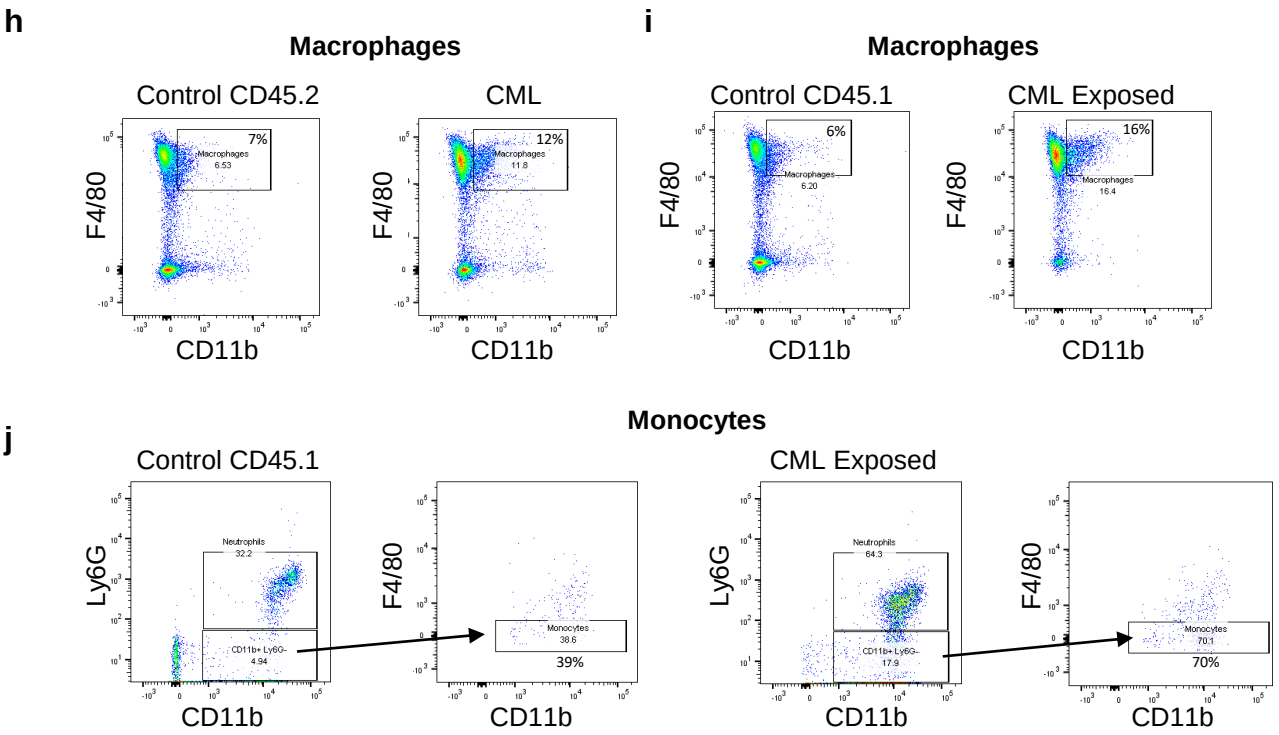


Fig. S2: Gating strategy and flow cytometry analysis of BM located myeloid cells and lymphocytes. a: Representative gating strategy for isolation of Lin$^-$ c-Kit$^+$ (LK) and Lin$^-$ c-Kit$^+$ Sca-1$^+$ and Lin-c-Kit$^+$ Sca-1$^+$ CD150$^+$ CD48$^-$ (LT-HSC) cells in CD45.1 BM. **b-j**: Representative flow cytometry plots of CD19$^+$ B cells (**b-c**), CD8$^+$ T cells (**d**), CD4$^+$ T cells (**e**), CD11b$^+$Ly6G$^+$ cells (**f-g**), CD11b$^+$F4/80$^+$ cells (**h-i**), and CD11b$^+$Ly6G$^-$F4/80$^-$ cells (**j**).

Supplemental Fig. S3

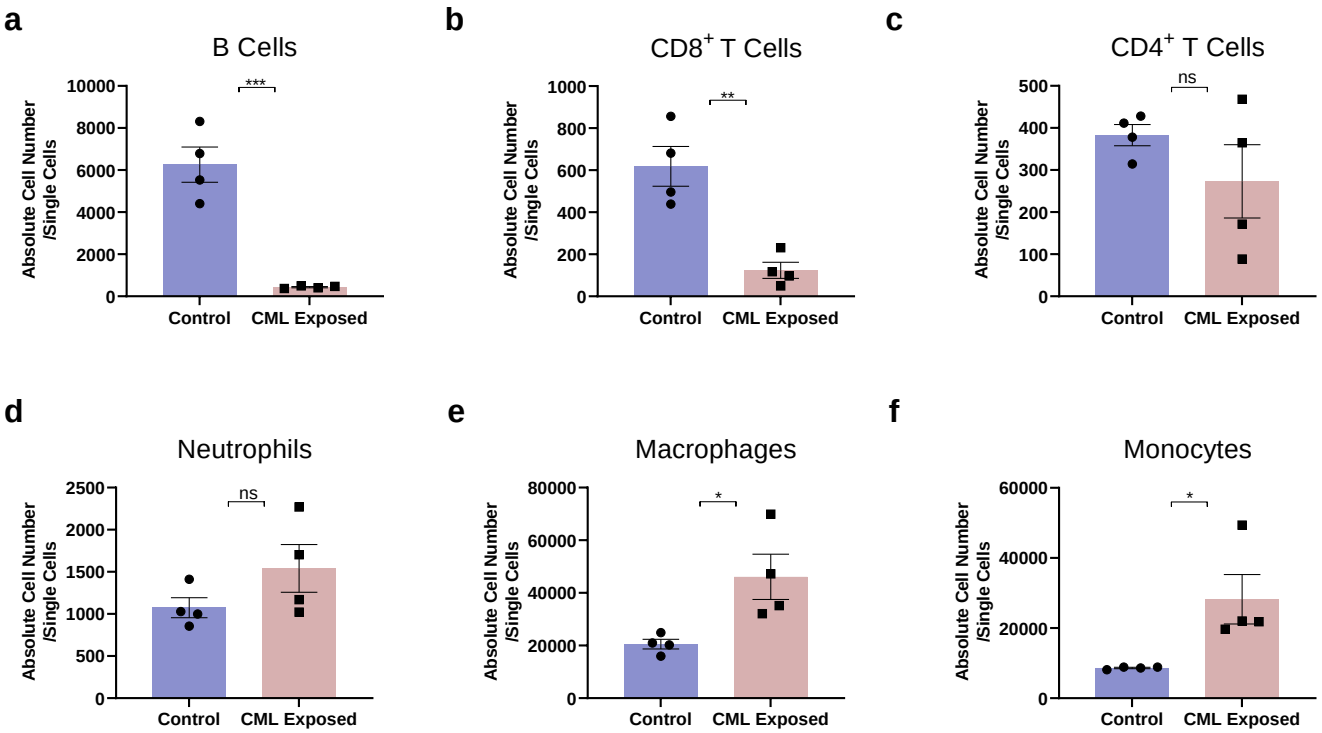


Fig. S3: Absolute cell numbers of control and CML exposed BM cell populations

Absolute cell numbers in BM in CD45.1 fraction of chimeric control or CML mice. Data representative of mean ± SD, N=4 mice per arm. Statistical analysis: unpaired Student's t-test, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Supplemental Fig. S4

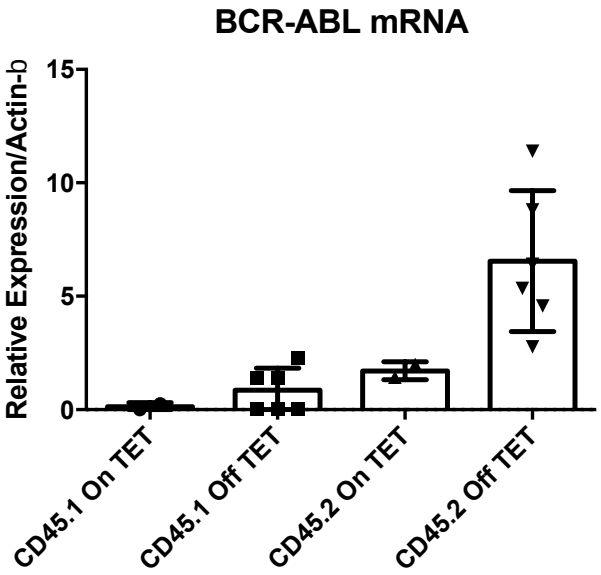
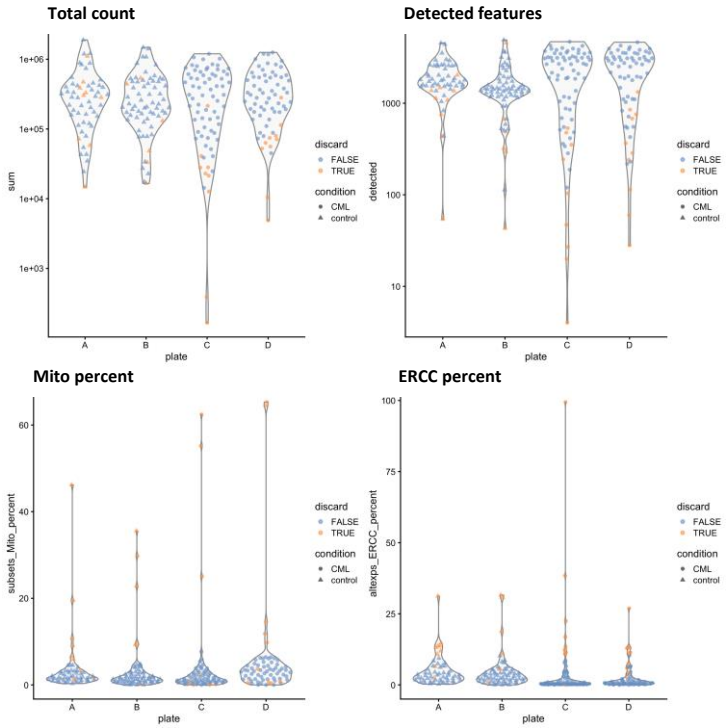


Fig. S4: BCR-ABL expression in macrophages from BM of CD45.1/CD45.2 chimeric mice.

RT-qPCR mRNA expression of BCR-ABL p210 in $CD11b^{+}$ $F4/80^{+}$ cells isolated from CD45.1 and CD45.2 BM fractions of mice maintained on or off tetracycline (TET) for 15 days, N=2-6 mice per arm.

Supplemental Fig. S5

a



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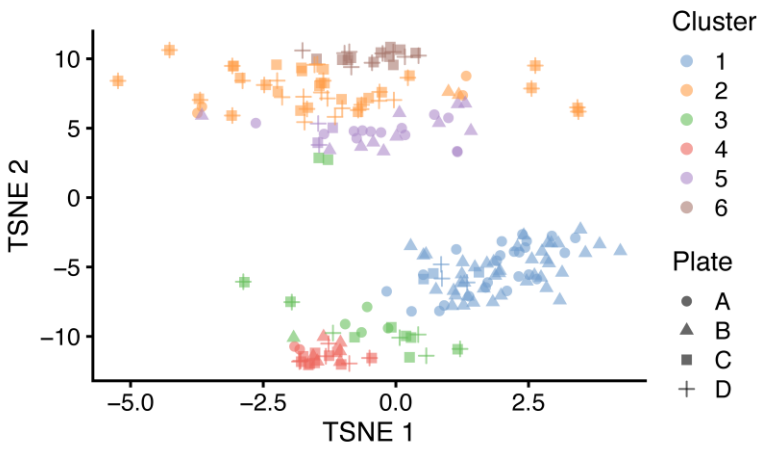

Fig. S5: sc-RNAseq QC plots

a: Quality control analysis of scRNAseq data showing total counts, features, mitochondrial and ERCC content. Orange denotes cells excluded from further analysis for not passing the QC threshold. ERCC threshold of 10.539%, mitochondrial content threshold of 8.433%, sum of counts threshold of 5137.281 and feature number threshold of 96.785. **(b)** t-SNE plot showing cell clustering according to plates processed.

Supplemental Fig. S6

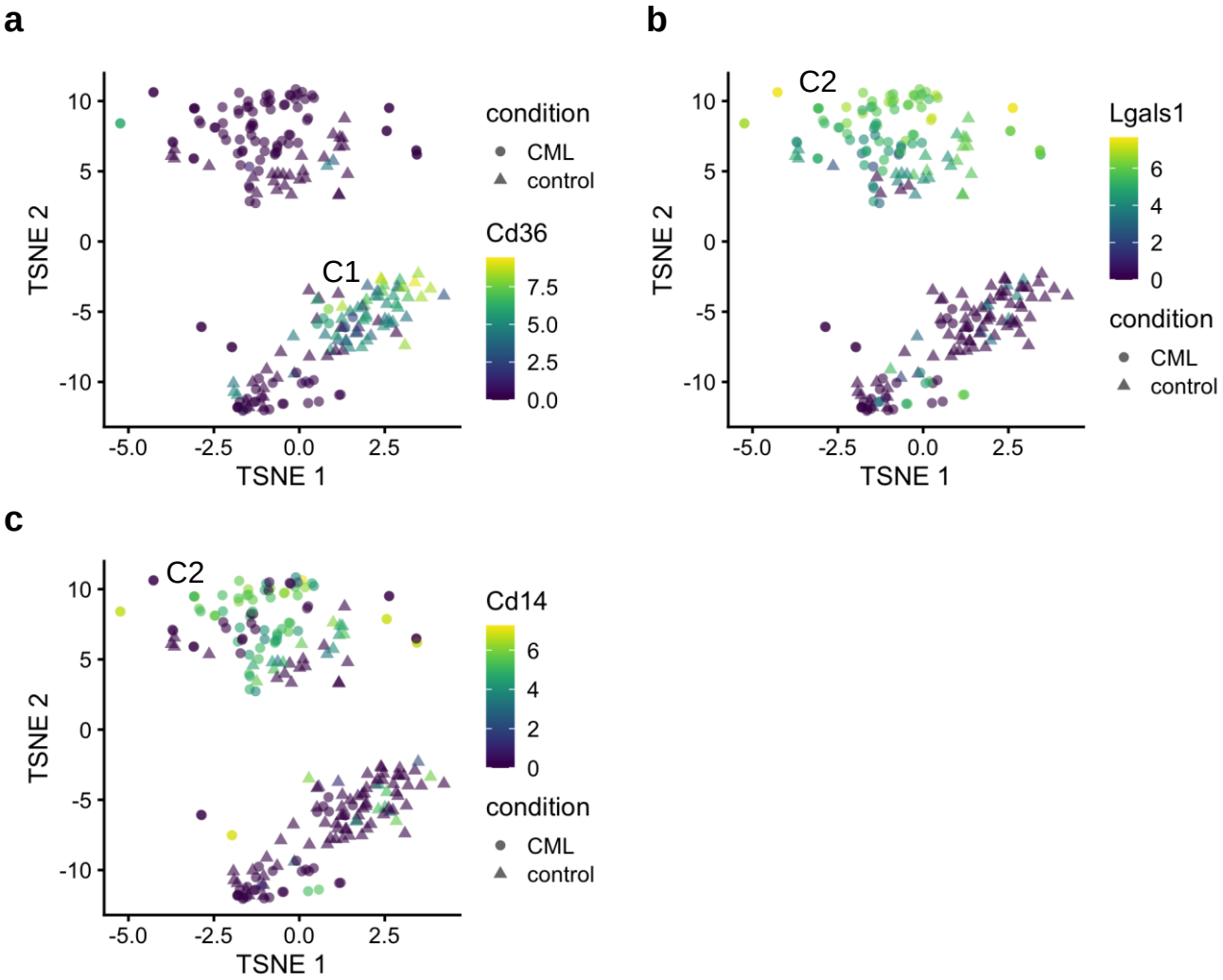

Fig. S6: CML Exposed Macrophages Express High *Lgals* and *CD14*, and Low *CD36* levels

Marker panel identification of single cell CD45.1^{+} CD11b^{+} F4/80^{+} RNA sequencing utilising COMET analysis. **a:** Cluster 1 *Cd36* enrichment. **b:** Cluster 2 *Lgals1* enrichment. **c:** Cluster 2 *Cd14* enrichment.

Supplemental Fig. S7

Fig. S7: Subpopulations of CML Exposed Macrophages Down Regulate Inflammatory Pathways. **a-c**: Pathway analysis of single cell clusters using Kegg, Reactome and Wikipathways. **a:** Cluster 2 downregulated pathways. **b**: Cluster 6 downregulated pathways. **c**: Cluster 1 upregulated pathways.

Supplemental Fig. S8

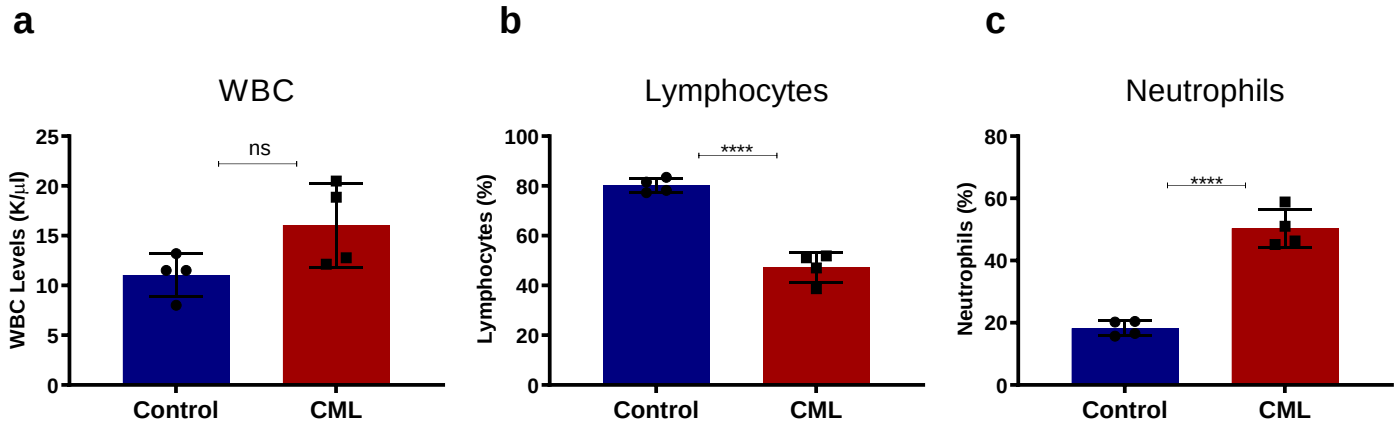

Fig. S8: Confirmation of CML disease in SCLtTA$^+$/BCR-ABL$^+$ murine model. Doxycycline was withdrawn from control and SCLtTA$^+$/BCR-ABL$^+$ mice for 8 weeks to induce CML disease; **a:** WBC levels (K/µl). **b:** lymphocytes (%). **c:** neutrophils (%). N = 4 mice per arm. Statistical analysis: unpaired Student's t-test, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Supplemental Fig. S9

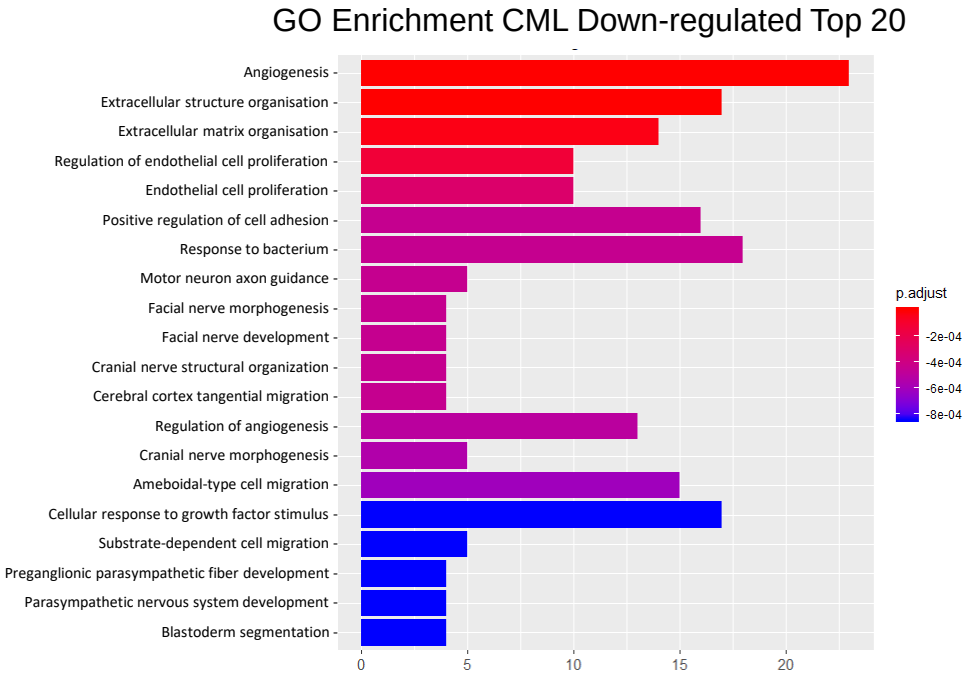

Fig. S9: Down-regulated pathways in GO enrichment analysis of murine CML LT-HSC RNA Sequencing

GO enrichment analysis of significant differentially expressed genes in CML LT-HSCs. LT-HSC differential expression calculated by DESeq2.

Supplemental Fig. S10

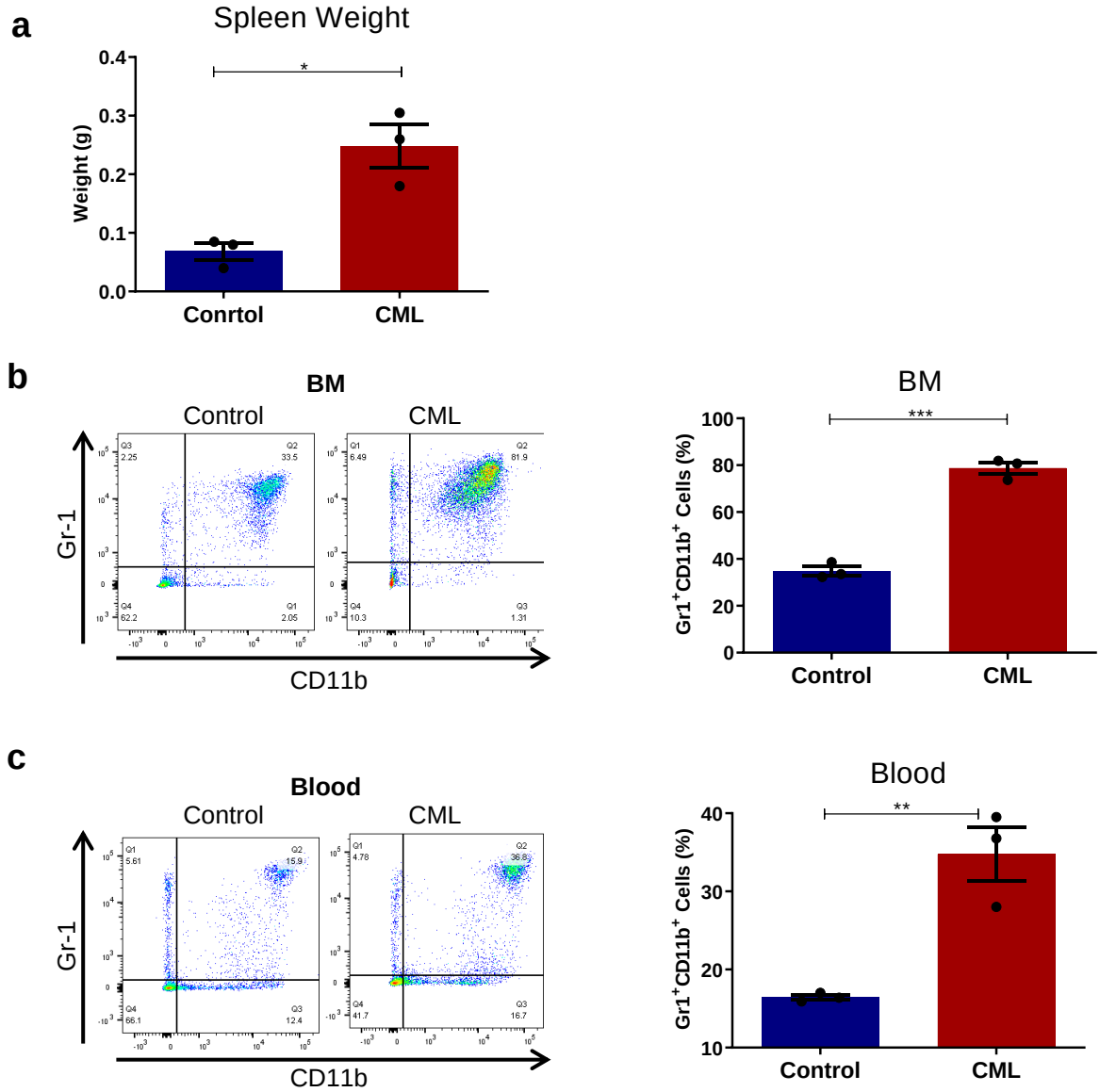

Fig. S10: Confirmation of CML disease in SCLtTA$^+$/BCR-ABL$^+$ murine model

Tetracycline was withdrawn from SCLtTA$^+$/BCR-ABL$^-$ and SCLtTA$^+$/BCR-ABL$^+$ mice for 15days to induce CML disease. **a:** Spleen weight (g) of control and CML mice (N=3 per arm). **b:** Percentage of Gr-1$^+$ CD11b$^+$ cells in BM of control and CML mice (N=3 per arm). **(c)** Percentage of Gr-1$^+$ CD11b$^+$ cells in blood of control and CML mice (N=3 per arm). Data representative of mean ± SEM. Statistical analysis: unpaired Student's t-test, * $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Supplemental Fig. S11

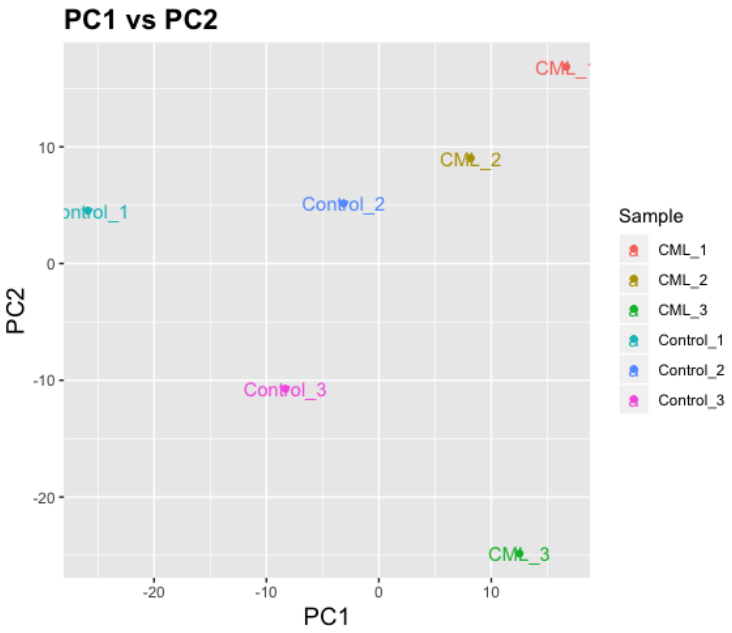

Fig. S11: Principal component analysis plot of murine c-kit$^+$ cell secretory proteome

Principle component analysis of label free quantification of secreted proteins from murine c-kit$^+$ cells cultured for 24hr. Control mice SCLtTA$^+$/BCR-ABL$^-$, N=3, CML mice SCLtTA$^+$/BCR-ABL$^+$, N=3. Data representative of principle component 1 (PC1) vs principal component 2 (PC2).

Supplemental Fig. S12

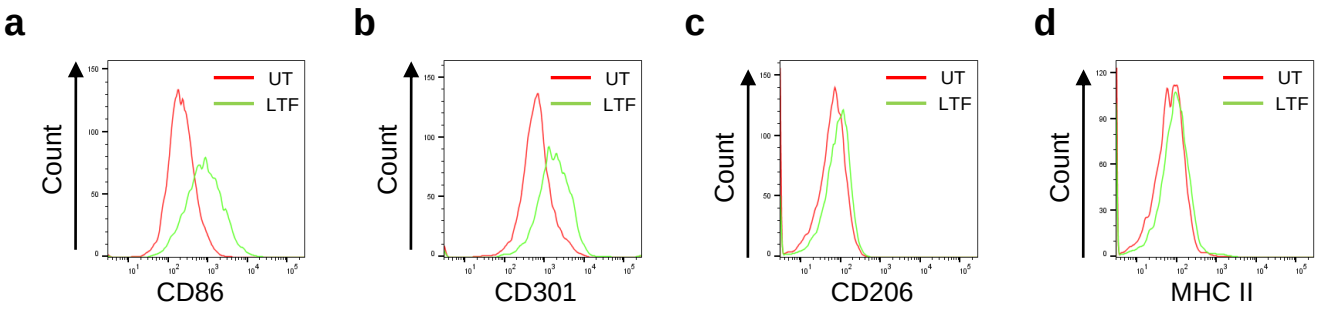

Fig. S12: Lactotransferrin Alters Bone Marrow Macrophage Phenotype. Cell surface maker expression of CD86 **(a)**, CD301 **(b)**, CD206 **(c)** and MHC II **(d)** on BMDM measured by flow cytometry. Representative histograms are shown of three independent experiments (N=3 per arm).