

Figure S1. Macrophage infiltration in DSS colitis. (A) Representative flow cytometry dot plots and **(B)** quantification of F4/80+/Cd11b+ cells in DSS colitis time course. *p<0.05.



Figure S2. Characterization of $LysM^{Cre}$; $Mcl1^{fl/fl}$ **mice. (A)** Representative flow cytometry dot plots of F4/80+/Cd11b+ cells in peripheral blood. (B) Representative H&E staining and (C) Ki67 immunofluorescence from $LysM^{Cre}$; $Mcl1^{wt/wt}$ and $LysM^{Cre}$; $Mcl1^{fl/fl}$ mouse colon tissue. (D) Cytokine array analysis from colon tissue lysates from $LysM^{Cre}$; $Mcl1^{wt/wt}$ (n=5) and $LysM^{Cre}$; $Mcl1^{fl/fl}$ (n=7).



Figure S3. Neutrophils are highly infiltrated in AOM/DSS colon tumors. (A) Representative flow cytometry dot plots and **(B)** quantification of Ly6g+/Cd11b+ cells in AOM/DSS colon tumors from WT mice. ****p<0.001. Statistical analysis performed by student's t test.



Figure S4. Tumor infiltration of macrophages is unaltered in *LysM^{Cre};Mcl1^{fl/fl}* **mice. (A)** Representative flow cytometry dot plots and (B) quantification of F4/80+/Cd11b+ cells in colon tumors from *LysM^{Cre};Mcl1^{wt/wt}* and *LysM^{Cre};Mcl1^{fl/fl}* mice. Statistical analysis performed by student's t test.



Figure S5. Monocytes are unchanged in *Mrp8-Cre/Mcl1*^{*fl/fl*} **mice.** (A) Representative flow cytometry dot plots and (B) quantification of Ly6c+/Cd11b+ cells as a percentage of total myeloid cells from $Mrp8^{Cre}$; *Mcl1*^{*wt/wt*} and $Mrp8^{Cre}$; *Mcl1*^{*fl/fl*} mice. Statistical analysis performed by student's t test.



Figure S6. PMN depletion increases microbiota-dependent inflammatory responses. (A) Western blot analysis of colon tumors from $LysM^{Cre};Mcl1^{wt/wt}, LysM^{Cre};Mcl1^{fl/wt}$, and $LysM^{Cre};Mcl1^{fl/fl}$ mice. Statistical analysis was performed with student's t-test. **(B)** NMDS plot based on θ_{YC} of $LysM^{Cre};Mcl1^{wt/wt}$ (WT) and $LysM^{Cre};Mcl1^{fl/fl}$ (KO) **(C)** β -diversity index, θ_{YC} of WT and KO mice. **(D)** Shannon's α -diversity index of WT and KO mice.



Figure S7. Bacteria and IL-17 are important for neutrophil-deficient colon tumorigenesis. (A) Representative images of immunofluorescence staining of p-H2AX in $LysM^{Cre};Mcl1^{wt/wt}$ and $LysM^{Cre};Mcl1^{tl/l}$ colon tumors treated with Ctrl or antibiotics (Abx). (B) ELISA analysis of IL-17 protein in colon tissue explants and (C) serum of mice treated with Ctrl IgG or IL-17 IgG (IL17i). **** p<0.001. (D) Tumor size of colon tumors in $LysM^{Cre};Mcl1^{wt/wt}$ and $LysM^{Cre};Mcl1^{tl/l}$ treated with Ctrl IgG or IL-17 IgG (IL17i). **** p<0.0001.



Figure S8. Increased B-cells in PMN-deficient colon tumors. (A) Flow cytometric analysis and **(B)** representative images of B220 staining of colon tumor tissue from $LysM^{Cre};Mcl1^{wt/wt}$ and $LysM^{Cre};Mcl1^{fl/fl}$ mice. **(C)** Flow cytometric analysis of B220 staining and **(D)** quantification of peripheral blood B-cells. **(E)** IgA ELISA analysis from feces of $LysM^{Cre};Mcl1^{wt/wt}$ and $LysM^{Cre};Mcl1^{fl/fl}$ mice. **(F)** Representative immunofluorescence of B220 staining from WT tumor tissue and invasive adenocarcinoma tissue from $LysM^{Cre};Mcl1^{fl/fl}$ mouse.



Figure S9. B-cell depletion does not exacerbate DSS colitis. (A) Schematic of 2.5% DSS treatment and anti-B220 injections (400ug/mouse I.P.) on days 1, 3, and 5. **(B)** Representative flow cytometric analysis of B220 staining in peripheral blood and colon tissue and **(C)** quantification B-cells of Ctrl and anti-B220 treated animals. **(D)** Representative H&E histologic analysis **(E)** colon length and **(F)** total inflammation score of treated mice. Statistical analysis performed by student's t test.



Figure S10. B-cell depletion reduces PMN-deficient tumor progression. (A) Tumor number and **(B)** representative histologic analysis indicated tumor stage from Ctrl and anti-B220 treated *LysM^{Cre};Mcl1^{fl/fl}* mice. Statistical analysis was performed by one-way ANOVA followed by Tukey's multiple comparisons test.