**Figure legends**

**Figure S1. Loss of CXCR2 in myeloid cells enhances anti-tumor immunity**

A, myeloid CXCR2 deficiency enhances the antitumor immunity phenotype. 7×105 Rich1.1 murine melanoma cancer cells were intravenously injected into CXCR2myeΔ/Δ (n=8) or littermate CXCR2WT mice (n=8). Twenty-six days after injection, the lung weight was determined and normalized to tumor-free lung. Data were analyzed statistically by the Two-sided t-test.

B, CXCL13 levels in tumor-bearing mice. Serum and tumor lysates were collected 7-days post intravenous implantation of 1×106 PyMT breast cancer cells into CXCR2myeΔ/Δ  and littermate CXCR2WT mice (n=6 samples per group). CXCL13 expression in the sera and lung tumor lysates were determined by ELISA assay (Cat#41907, Biolegend). Data were analyzed statistically by the Student’s two-sided t-test.

C, Peripheral CD45+ cell number in tumor-free/bearing CXCR2WT mice and CXCR2myeΔ/Δ mice (n=6).

D, strategy to sort potential MDSC cells. The knock in mT/mG gene served as a myeloid specific LysM reporter strain and after Cre-mediated recombination, myeloid cells are green in the CXCR2myeΔ/Δ  and the CXCR2WT mice. The green myeloid cells were further sorted as potential G-MDSC (Ly6C-Ly6G+) and M-MDSC (Ly6G-Ly6C+) cells.

E, strategy for sorting the CD4+ T cell subpopulation. CD45+CD3+CD4+ staining cells were subsequently further analyzed as Treg (CD25+) cells, naïve T cells (CD62L+) cells, or Tm (effector/memory) TEM cells (CD44+) cells.

**Figure S2. Peripheral immune profile in the melanoma tumor-bearing mice**

CXCR2WT and littermate CXCR2myeΔΔ mice were intravenously implanted with PyMT cells, and eight days after implantation peripheral blood leukocytes were isolated from both CXCR2myeΔ/Δ or CXCR2WT mice and analyzed by multicolor FACS (A-D, L). A, MHC II expressing macrophages from peripheral blood expressed as a percent of CD11b + cells. comparison to total CD11b+ cells; B, G- and M-MDSCs as a percent of total CD11B+ cells in peripheral blood. C, a representative graph of CXCR2 expression on G-MDSC and M-MDSC cells. D, CD4+ and CD8+ T cells as a percent of CD3+CD45+ cells in peripheral blood and E, effector memory CD4+ T cells in CXCR2myeΔ/Δ or CXCR2WT mice. Data were analyzed statistically using the two-sample t-test with unequal variances where p<0.01 for CXCR2myeΔ/Δ vs.CXCR2WT mice. (F-K) Mice were intravenously implanted with Rich1.1 melanoma tumor cells and 8 days after implantation leukocytes from peripheral blood were analyzed by multicolor FACS. F, the peripheral macrophages expressing MHC II; G, peripheral MDSC populations [G-MDSC (Ly6C-Ly6G+) and M-MDSC (Ly6G-Ly6C+) cells]; H, CD4+ and CD8+T cell populations; I, memory/effector CD4+ T cells; J, CD8+ T cells that stained positively for CD103 or PD-1; K, B cells (CD19+B220+cells) in CXCR2myeΔ/Δ or CXCR2WT mice. L, total CD45+ cell number/100 mg tissue in tumor- bearing CXCR2WT mice and CXCR2myeΔ/Δ mice (n=8). Data were analyzed statistically using the Student’s t-test where p<0.01 is CXCR2myeΔ/Δ vs.CXCR2WT mice.

**Figure S3, Analysis of tumor-infiltrated immune cells**

7×105 Rich1.1 mouse melanoma cells were intravenously injected into CXCR2myeΔ/Δ (n=8) or littermate CXCR2WT mice (n=8). Two weeks after injection, the infiltrated leukocytes in the lung tumors were stained with specific antibodies and analyzed by FACS to identify A, M1 macrophages (GFP+F4/80+MHC II+) or M2 macrophages (GFP+F4/80+CD206+); B, potential G-MDSCs (Ly6C-Ly6G+) or M-MDSCs-(Ly6G-Ly6C+); C, NK cell (CD45+CD3-NK1.1) surface markers CD107a and CD178; D, CD4+T cells of memory/effector (CD62L-CD44+), naïve (CD44-CD62L+) or Treg (CD25+) lineage; E, mDC1 (CD45+ /GFP-/CD11c+/MHC II+/CD103+) and F, CD8+ T cell surface markers CD103, CD107a and PD-1.

**Figure S4, MDSCs inhibit CD8+ T cell cytotoxicity *ex vivo*.**

A, depletion of CD8+ T cells in CXCR2WT mice.C57Bl6 mice (5/group) were injected intra-peritoneally with CD8a mAb or control IgG daily for the first three days then maintained twice weekly. After the first three days of antibody treatment, mice were injected intravenously with 1x106 PyMT cells. Two weeks after tumor cells were implanted, the mice were sacrificed, and the weight of the tumor-bearing lung was measured. ns refers to “no statistical difference” between compared groups.

B, MDSCs from tumor-bearing lungs of CXCR2myeΔ/Δ or CXCR2WT mice and CD8+ T cells from lung tumor of CXCR2WT mice were co-cultured with PyMT-luc cells at the indicated ratio. After 3 days of co-culture, the luciferase activity of the remaining viable cells was measured and CD8 T cell killing activity was calculated as described in Methods.

**Figure S5, cytokine array on serum samples**

A, the sera of tumor-free mice were subjected to cytokine array (5 mice per group).

B, the sera of tumor-bearing mice were subjected to cytokine array (5 mice per group).

Table S2, 62 cytokines were listed.

C, CXCL11 levels in lung in tumor-free mice were determined by ELISA (5 mice per group).

D, CXCL11 levels in spleen in tumor-free mice were determined by ELISA (5 mice per group).

E, CXCL11 in serum in tumor-free mice were determined by ELISA (5 mice per group).

F, CXCL11 expression in tumor cells. PyMT breast cancer cells (2×105) and Rich1.1 melanoma (2×105) were cultured in 1.5 ml DMEM/F-12 medium in 6-well/plates (n=5 per cell line). After two days of culture, the supernatant CXCL11 level was determined by ELISA.

G, CXCL11 levels in tumors of mice after B cell depletion. CXCR2myeΔ/Δ mice were injected intraperitoneally with 200µg/B220 mAb or IgG control daily for 3 days prior to intravenous implantation with 1×106 PyMT breast cancer cells (n=5 mice per group). The B cell depletion was maintained by 200µg/B220 mAb every other day, and control IgG groups continued to receive treatment every other day. Tumor volume was measured weekly and seventeen days after implantation of tumor cells, mice were euthanized and CXCL11 expression in the tumor lysates was determined by ELISA. Data were analyzed statistically by the Student’s two-sided t-test.

**Figure S6, B cells impact on anti-tumor immunity through CXCL11**

A, strategy for sorting the B cell subpopulation: B cells: CD19+B220+ cells; B1 cells: CD19+B220+CD43+ cells; B2 cells: CD19+B220+CD43- cells; Pre-B cells: CD19+B220-CD43- cells; B1a cells: CD19+B220+CD5+ cells; B1b cells: CD19+B220+CD5- cells.

B, CXCL11 was differentially expressed by subsets of immune cells in the TME. CXCR2myeΔ/Δ (n=8).

C, percentage of peripheral B cell subpopulation distributed. 1×106 PyMT breast cancer cells were intravenously injected into CXCR2myeΔ/Δ (n=8) or littermate CXCR2WT mice (n=8). Two weeks after injection, sub-populations of B cells in the TME were analyzed by FACS.

D, Intracellular CXCL11 expression in subsets of peripheral B cells was determined by FACS.

E, CXCL11 chemotaxis to CD8+T cells. CD8+T cells were negatively isolated from spleen of tumor-bearing mice and analyzed for chemotactic response to increasing concentrations of CXCL11 using a Boyden Chamber Assay. Data are representative of duplicate assays.

F, B cell ratio in CXCR2WT mice. FACS analysis for lung sub-population of B cells in the CXCR2WT mice (n=8) with tumor outgrowth in the lung (T) or without tumor in the lung (N).

G, B cell ratio in CXCR2myeΔ/Δ mice. FACS analysis for sub-population of B cells in the lungs of CXCR2myeΔ/Δ mice (n=8) with tumor (T) or without tumor (N) outgrowth in the lung.

H, B cell chemotaxis assay. 50,000 B cells isolated from tumor tissue of CXCR2WT mice were added with or without 20 nM SCH546738 into the top wells of the chemotaxis chamber. The bottom chamber contains 100 µl of media with or without 1µg/ml rCXCL11. After 24h of incubation, the B cells that migrated into the bottom chamber were counted by flow cytometry.

I, B cell chemotaxis assay. 50,000 B cells from tumor tissue of CXCR2myeΔ/Δ mice were added with or without 20 nM SCH546738 into the top wells of the chemotaxis chamber. The bottom chamber contained 100 µl of media with or without 1µg/ml rCXCL11. After 24h of incubation, the B cells of bottom chamber were counted by flow cytometry. n=4. The experiment was repeated, and the two sets of experimental data were pooled together for statistical analysis.

J. Mouse body weight. C57/BL6 mice were allowed free access to chow containing SX-682 or vehicle control chow from one week prior to subcutaneous implantation with Rich1.1 melanoma cells (1×106), and thereafter for the duration of the experiment. Body weight was measured and recorded weekly.