

Figure S1. Unaltered phagocytosis in SP140 deficient macrophages, Related to Figure 1. (A) Representative histogram overlay of pHrodo Green fluorescence (left) and percentage (right) of phagocytosing mouse bone marrow-derived macrophages (BMDMs) from WT and *Sp140*^{-/-} mice. **(B)** Representative histogram overlay of pHrodo Green fluorescence (left) and percentage (right) of phagocytosing THP-1 human monocytes treated with control (Ctrl) or *SP140* targeting siRNAs. Data are mean of three biological replicates, error bars are SEM. ns is not significant; unpaired t-test.

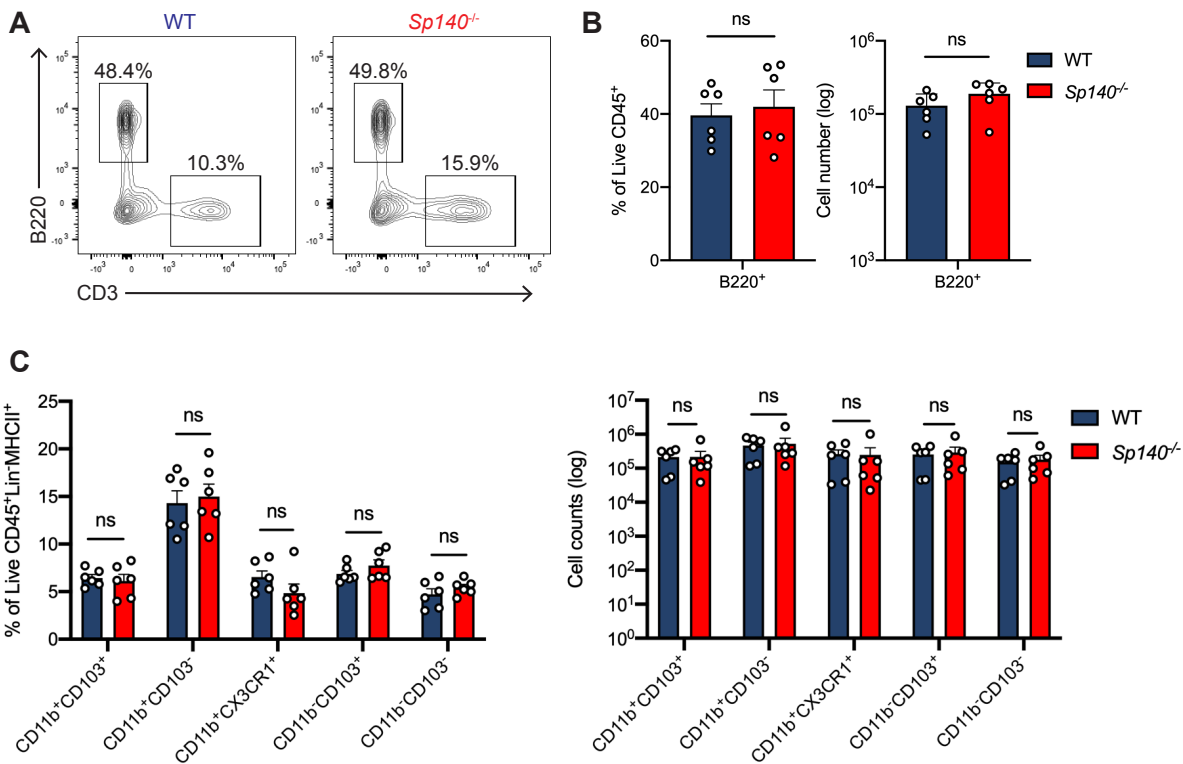


Figure S2. Characterization of leukocyte populations in WT and *Sp140*^{-/-} mouse colon lamina propria at homeostasis, Related to Figure 1. (A) Representative flow cytometry plots of live CD45⁺ cells gated on B220⁺ and CD3⁺ populations. **(B)** Quantification of frequency and total count of B220⁺ B cells. **(C)** Quantification of frequency and total count of mononuclear phagocytes. Data are mean of six biological replicates, error bars are SEM. ns is not significant; unpaired t-test.

Table S1. Patient metadata including age, remission status, and medication at time of stool collection for healthy control, CD patients expressing wildtype SP140 (SP140^{wt}), and CD patients bearing the common SP140 genetic variant (SP140^{mut}). Related to Figure 4.

Diagnosis	PUB ID	Sex	Age at Diagnosis	Age at Collection	In Remission ?	Medication at Time of Collection
Healthy Control <i>SP140^{wt}</i>	160826	F	N/A	46	N/A	N/A
	120777	M	N/A	22	N/A	N/A
	107560	F	N/A	22	N/A	N/A
Crohn's Disease <i>SP140^{wt}</i>	109307	F	10	23	Yes	Remicade
	110577	F	38	38	No	Mesalamine
	138741	M	21	43	Yes	Ciprofloxacin, Budesonide, Mercaptopurine, Humira
Crohn's Disease <i>SP140^{mut}</i>	159126	F	46	60	No	Prednisone, Simponi
	184102	F	61	66	Yes	Prednisone
	160916	F	15	37	Yes	Cimzia