

Table S1. Summary of clinical characteristics, colitis onset, and treatment history of patient groups included in scRNA-seq analysis, Related to Figure 1.

	Ipilimumab (or combination)		Control (N=8)
	Colitis (N=8)	No Colitis (N=6)	
Age	64.2 (49 – 78)	59.0 (43 – 75)	50.9 (21-70)
M:F	4:4	2:1	5:3
Malignancy			
melanoma	8	6	1
other	0	0	1
Stage			
4	8	6	0
3	0	0	0
1-2	0	0	2
Current Immunotherapy			
Ipilimumab	2	1	NA
Ipilimumab + Nivolumab	6	4	NA
Prior Immunotherapy			
Ipilimumab	0	1	NA
PD-1/PD-L1	6	4	NA
Ipilimumab + Nivolumab	0	1	NA
None	2	2	NA
Average Treatment Cycles (mean +/- sd)	2.4 +/- 0.9	1.4 +/- 0.5	NA
Time from first treatment to symptoms (days) (mean +/- sd)	47.4 +/- 24.9	18.0 +/- 13.9	NA
Time from last cycle to symptoms (days) (mean +/- sd)	15.6 +/- 5.7	10.0 +/- 3.9	NA
Time from symptom onset to endoscopy (days) (mean +/- sd)	4.5 +/- 4.8	3.6 +/- 1.5	NA
Diagnosis			
Colitis	5	0	0
Enterocolitis	3	0	0
Enteritis	0	3	0
No inflammation	0	3	9
Colitis Severity (MES)	1.6 (range 1-2)	0	0
CTCAE Grade	2.5 (range 1-4)	1.2 (range 0-2)	0
Steroids prior to endoscopy	1/8	0/6	0/9
Response to corticosteroids	3/8	1/3	NA
Received Infliximab	4/8	2/3	NA
Additional irAE	4/8	3/5	

Table S2. CPI treatment history for each patient included in scRNA-seq studies, Related to Figure 1.

Patient ID	Treatment	Age	Sex	Malignancy	Stage	Prior Tx	Time from last Tx (months)
C1	Ipilimumab	62.0	F	Melanoma	4	Pembro	0.5
C2	Ipilimumab	71.2	F	Melanoma	4	Pembro	7
C3	Ipilimumab + Nivolumab	56.2	M	Melanoma	4	Pembro	0.5
C4	Ipilimumab + Nivolumab	61.5	M	Melanoma	4	Nivo	0.5
C5	Ipilimumab + Nivolumab	72.8	M	Melanoma	4	none	NA
C6	Ipilimumab + Nivolumab	78.4	M	Melanoma	4	none	NA
C7	Ipilimumab + Nivolumab	61.6	F	Melanoma	4	Pembro	24
C8	Ipilimumab + Nivolumab	49.5	F	Melanoma	4	Pembro	1
NC1	Ipilimumab + Nivolumab	43.6	M	Melanoma	4	none	NA
NC2	none	68.1	M	Melanoma	4	Pembro, Ipi	1
NC3	Ipilimumab	70.5	F	Melanoma	4	Pembro, Durva	12
NC4	Ipilimumab + Nivolumab	63.7	M	Melanoma	4	none	NA
NC5	Ipilimumab + Nivolumab	58.5	M	Melanoma	4	Nivo, Ipi+Nivo	1
NC6	Ipilimumab + Nivolumab	49.3	F	Melanoma	4	Pembro	2
CT1	NA	21.4	F	melanoma	1A		
CT2	NA	61.7	M				
CT3	NA	50.5	M				
CT4	NA	43.4	M				
CT5	NA	70.6	F	gastric	2		
CT6	NA	44.3	M				
CT7	NA	50.2	M				
CT8	NA	61.5	F				

Table S3. Characteristics of colitis development and clinical management for each patient included in scRNA-seq studies, Related to Figure 1. * Patient NC2 had terminated CPI therapy 1 month prior to endoscopy.

	Diagnosis	Diarrhea Grade (CTCAE)	Mayo Endoscopic Score (MES)	Time from first treatment to symptom onset (days)	Time from most recent cycle to symptom onset (days)	Time from symptom onset to biopsy (days)	Total treatment cycles	Steroids prior to endoscopy	Infliximab Required for Treatment
C1	colitis	2	1	8	8	0	1	no	no
C2	colitis	2	1	57	15	13	3	no	no
C3	colitis	3	2	83	26	6	3	yes	yes
C4	entero-colitis	2	2	63	19	2	3	no	yes
C5	entero-colitis	1	2	59	10	10	3	no	yes
C6	entero-colitis	3	1	56	15	3	3	no	no
C7	colitis	4	2	19	19	1	1	no	yes
C8	colitis	3	2	34	13	1	2	no	no
NC1	enteritis	1	0	35	16	2	2	no	no
NC2*	normal	0	0	NA	NA	NA	NA	no	NA
NC3	enteritis	2	0	31	10	5	2	no	yes
NC4	normal	1	0	7	7	5	1	no	NA
NC5	enteritis	1	0	11	11	4	1	no	yes
NC6	normal	2	0	6	6	2	1	no	NA
CT1	normal	0	0	NA	NA	NA	NA	NA	NA
CT2	normal	0	0	NA	NA	NA	NA	NA	NA
CT3	normal	0	0	NA	NA	NA	NA	NA	NA
CT4	normal	0	0	NA	NA	NA	NA	NA	NA
CT5	normal	0	0	NA	NA	NA	NA	NA	NA
CT6	normal	0	0	NA	NA	NA	NA	NA	NA
CT7	normal	0	0	NA	NA	NA	NA	NA	NA
CT8	normal	0	0	NA	NA	NA	NA	NA	NA

Table S4. Tumor response rate and durations for CPI-treated patients for each patient included in scRNA-seq studies, Related to Figure 1. RECIST response definitions: PD= progressive disease, PR= partial response, SD= stable disease. * Patient NC2 had terminated CPI therapy 1 month prior to endoscopy.

	Diagnosis	RECIST response (best response at time of endoscopy)	Overall Survival (months) from CPI initiation to date of death	Current status (April 2020)
C1	colitis	PD	4.2	deceased
C2	colitis	PR	13.0	deceased
C3	colitis	PR	17.5	alive
C4	entero-colitis	PD	6.1	deceased
C5	entero-colitis	SD	13.9	alive
C6	entero-colitis	PR	13.2	alive
C7	colitis	PD	5.7	deceased
C8	colitis	PD	11.1	deceased
NC1	enteritis	PR	17.5	alive
NC2	normal	*	*	alive
NC3	enteritis	PD	15.1	alive
NC4	normal	PR	12.6	alive
NC5	enteritis	PD	12.3	deceased
NC6	normal	PD	10.4	alive