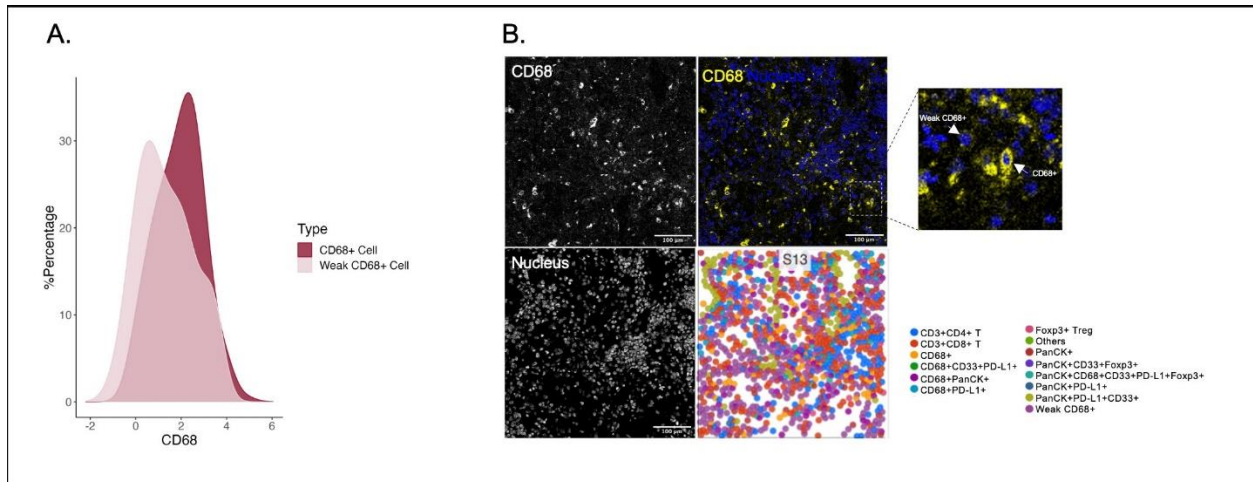


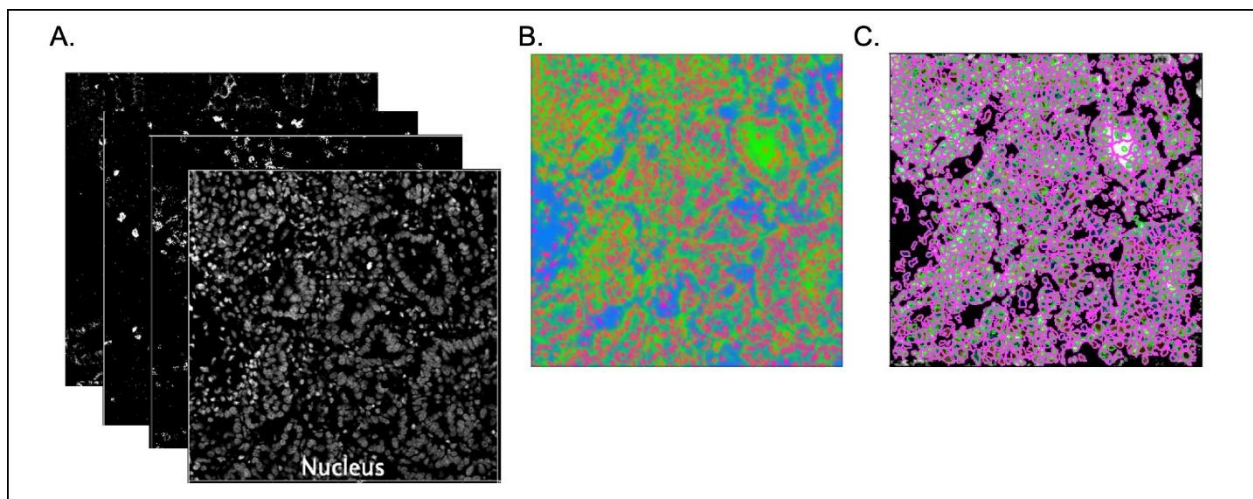
Supplemental Figure 1. Marker Intensity and Cell Annotation

A. Marker intensity per cell type. **B.** Z-score of marker intensity per cell type. **C.** Uniform Manifold Approximation and Projection (UMAP) color by marker intensity per cell.



Supplemental Figure 2. The CD68 intensity for CD68+ cell and weak CD68+ cell

A) The CD68 Intensity for CD68+ cell and Weak CD68+ Cell; **B)** The CD68+ cell and Weak CD68+ cell on the IMC images and cell annotation map.



Supplemental Figure 3. Cell segmentation. A) The combination of markers for cell membrane and cell nuclear; **B)** The probability RGB image for cell nuclear (red), cell membrane (green), and background (blue); **C)** the cell segmentation analysis result overlaps with cell membrane probability image. The green line labels the nuclear and the purple line separates the cells.

Supplemental Table 1. Treatment table

Sample name	Immunotherapy	Combination or Monotherapy
S01	Atezolizumab	Monotherapy
S02	Nivolumab	Monotherapy
S03	Atezolizumab	Monotherapy
S04	Pembrolizumab	carboplatin, pemetrexed
S05	Pembrolizumab	Monotherapy
S06	Pembrolizumab	carboplatin, pemetrexed
S07	Nivolumab	Monotherapy
S08	Nivolumab	Monotherapy
S09	Pembrolizumab	Monotherapy
S10	Atezolizumab	Monotherapy
S11	Atezolizumab	Monotherapy
S12	Atezolizumab	Monotherapy
S13	Atezolizumab	Monotherapy
S14	Atezolizumab	Monotherapy
S15	Nivolumab	Monotherapy
S17	Nivolumab	Monotherapy
S18	Nivolumab	Monotherapy
S19	Nivolumab	Monotherapy
S20	Pembrolizumab	Monotherapy
S21	Atezolizumab	Monotherapy
S22	Atezolizumab	Monotherapy
S23	Pembrolizumab	Monotherapy
S24	Pembrolizumab	carboplatin, pemetrexed
S25	Pembrolizumab	Monotherapy
S26	Pembrolizumab	carboplatin, pemetrexed

Supplemental Table 2. Immunotherapy responses

Immunotherapy	PD	PR	p-value
Atezolizumab	5 (41.7%)	4 (30.8%)	0.85

Nivolumab	3 (25.0%)	4 (30.8%)
Pembrolizumab	4 (33.3%)	5 (38.5%)

Supplemental Table 3. Genomic Variation Associated with Response Status

		PD	PR	p-value*
TP53	Negative	6 (60.0%)	8 (61.5%)	1
	Mutated	4 (40.0%)	5 (38.5%)	
LRP1B	Negative	1 (25.0%)	4 (80.0%)	0.33
	Mutated	3 (75.0%)	1 (20.0%)	
SPTA1	Negative	4 (100.0%)	4 (80.0%)	1
	Mutated	0	1 (20.0%)	
ARID1B	Negative	3 (75.0%)	5 (100.0%)	0.906
	Mutated	1 (25.0%)	0	
SMARCA4	Negative	2 (40.0%)	6 (100.0%)	0.122
	Mutated	3 (60.0%)	0	
MLL3	Negative	3 (75.0%)	4 (80.0%)	1
	Mutated	1 (25.0%)	1 (20.0%)	
STK11	Negative	8 (80.0%)	13 (100.0%)	0.347
	Mutated	2 (20.0%)	0	
EPHA3	Negative	3 (75.0%)	6 (100.0%)	0.83
	Mutated	1 (25.0%)	0	
KEAP1	Negative	2 (40.0%)	6 (100.0%)	0.122
	Mutated	3 (60.0%)	0	
NKX2_1	Negative	3 (75.0%)	5 (83.3%)	1
	Mutated	1 (25.0%)	1 (16.7%)	
MLL	Negative	3 (75.0%)	5 (100.0%)	0.906
	Mutated	1 (25.0%)	0	
FAT1	Negative	4 (100.0%)	3 (60.0%)	0.53

	Mutated	0	2 (40.0%)	
ATM	Negative	9 (100.0%)	10 (76.9%)	0.358
	Mutated	0	3 (23.1%)	
NF1	Negative	4 (100.0%)	5 (83.3%)	1
	Mutated	0	1 (16.7%)	
CDKN2AB	Negative	4 (66.7%)	6 (100.0%)	0.439
	Mutated	2 (33.3%)	0	
TSC2	Negative	5 (83.3%)	6 (85.7%)	1
	Mutated	1 (16.7%)	1 (14.3%)	
TET2	Negative	3 (75.0%)	6 (100.0%)	0.83
	Mutated	1 (25.0%)	0	
ARID2	Negative	3 (75.0%)	4 (80.0%)	1
	Mutated	1 (25.0%)	1 (20.0%)	
CDKN2A	Negative	8 (88.9%)	12 (92.3%)	1
	Mutated	1 (11.1%)	1 (7.7%)	
BRCA2	Negative	9 (100.0%)	12 (92.3%)	1
	Mutated	0	1 (7.7%)	
MYC	Negative	7 (87.5%)	8 (100.0%)	1
	Mutated	1 (12.5%)	0	
ARID1A	Negative	7 (87.5%)	4 (57.1%)	0.459
	Mutated	1 (12.5%)	3 (42.9%)	
AR	Negative	7 (87.5%)	7 (100.0%)	1
	Mutated	1 (12.5%)	0	
MLL2	Negative	3 (75.0%)	5 (100.0%)	0.906
	Mutated	1 (25.0%)	0	
PIK3CA	Negative	8 (88.9%)	13 (100.0%)	0.85
	Mutated	1 (11.1%)		
PRKDC	Negative	4 (80.0%)	5 (100.0%)	1
	Mutated	1 (20.0%)	0	

NOTCH1	Negative	9 (100.0%)	12 (92.3%)	1
	Mutated	0	1 (7.7%)	
EGFR	Negative	11 (91.7%)	12 (92.3%)	1
	Mutated	1 (8.3%)	1 (7.7%)	
APC	Negative	9 (90.0%)	13 (100.0%)	0.893
	Mutated	1 (10.0%)	0	
FANCA	Negative	6 (100.0%)	6 (85.7%)	1
	Mutated	0	1 (14.3%)	

*Chi-square test. **PD**: progression of disease. **PR**: partial response.

Supplemental Table 4. KRAS Variation Subtypes with Response Status

KRAS Variations	PD	PR	p-value*
G12A	0	2 (15.4%)	0.485
G12C	5 (41.7%)	3 (23.1%)	
G12D	2 (16.7%)	2 (15.4%)	
G12V	2 (16.7%)	2 (15.4%)	
Q61H	0	2 (15.4%)	
Q61L	1(8.3%)	0	
others	2 (16.7%)	2 (15.4%)	

*Chi-square test. **PD**: progression of disease. **PR**: partial response.

Supplemental Table 5. Antibody Panel

Target	Metal	Material ID*
CD3	170Er	3170019D
CD4	156Gd	3156033D
CD8	162Dy	3162035D
FOXP3	155Gd	3155016D
CD68	159Tb	3159035D
Arginase-1	164Dy	3164027D
CD33	145Nd	3145017D
HLA-DR	174Yb	3174023D
PanCK	148Nd	3148020D
PD-1	165Ho	3165039D
PD-L1	150Nd	3150031D

*Fluidigm Corporation (South San Francisco, CA). **PD**: progression of disease. **PR**: partial response.

Supplemental Table 6. Cell population by type and percentage

Cell Type	Cell Count	Percentage
CD4 T Cell	1409	6.6%
CD68	4397	20.7%
CD68+CD33+PDL1	451	2.1%
CD68+PanCK	623	2.9%
CD68+PDL1	1501	7.1%
CD8 T Cell	3326	15.7%
Foxp3+ Treg Cell	802	3.8%
PanCK	1720	8.1%
PanCK+CD33+Foxp3	4790	22.6%
PanCK+CD68+CD33+PDL1+Foxp3	950	4.5%
PanCK+PDL1	1555	7.3%
PanCK+PDL1+CD33	980	4.6%
weak CD68	4697	22.1%
others	13	0.1%