Supplementary Figure 1. Flow cytometry panels used for BD Canto (**A**) and BD Fortessa (**B**).

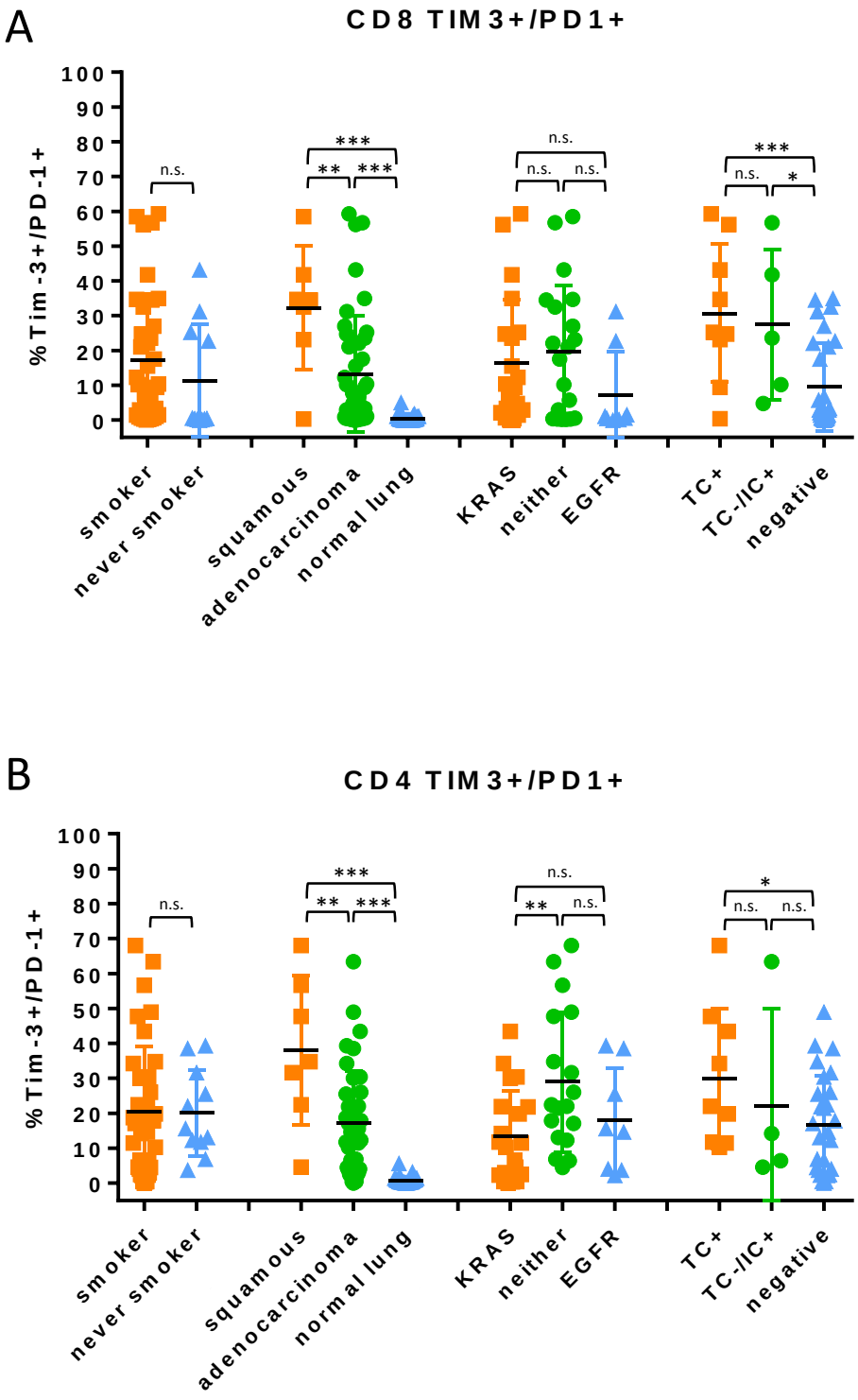
A

		Name	ID	*Fluorochrome*						
				AF488	PE	PerCp-Cy5.5	APC	PacBlue	PE-Cy7	APC-H7
Immune Analysis	Surface	Lympho*	1	CD56	**CD8**	CD16	**CD3**	CD45	CD19	CD4
		T1*	2	CD4	CD38	**HLA-DR**	CD45RA	CCR7	CD3	CD8
		T2	3	CD45	Tim-3	CD8	**LAG3**	CD3	PD-1	CD4
		T2 iso	4	CD45	iso	CD8	**iso**	CD3	iso	CD4
		T3	5	CD4	Tim3	CD8	CD45RO	CD3	PD-1	CD45RA
		T4	6	**CD11a**	**CD69**	CD8	CXCR3	CD3	PD-1	CD4
		Myelo*	7	CD45	CD66b	**HLA-DR**	CD33	CD14	CD123	CD16
		Tumor*	8	CD45	PD-L2	CD66b	PD-L1	CD33	EpCAM	CD14
		Tumor iso*	9	CD45	iso	CD66b	iso (PD-L1)	CD33	EpCAM	CD14
	Intra	T1	10	CD45	CTLA-4	CD8	FOXP3	CD3	PD-1	CD4
		T2	11	CD45	iso	CD8	FOXP3	CD3	iso	CD4
		T3	12	CD45	Tim-3	CD8	FOXP3	CD3	Ki67	CD4
Sorting			1	CD45	CD56	CD8	CD33	EpCAM	CD4	CD16

B

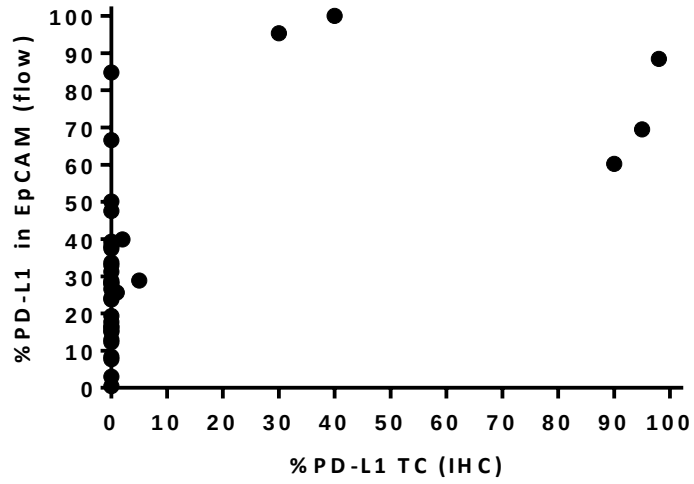
Ab	FITC	PerCP Cy5.5	PE	PE-CF594	PE/Cy7	APC	Alexa 700	APC/Cy7	BV421	BV510	BV605	BV711	BV780
Lymphocytes	IL-10	CD8	CXCR5	CD56	CD25	FoxP3	CD3	L/D	PD-1	CD40L	Ki67	CD45	CD4
T cells	CD69	CD8	CD38	CCR7	CTLA-4	TIM-3	CD3	L/D	PD-1	CD45RA	CD45RO	CD45	CD4
Myeloid	CD16	CD33	PD-L2	CD163	CD83	PD-L1		L/D	HLA-DR	CD15	CD123	CD45	CD14
B cells	IL-10	CD21	CD38	CD27	CD19	PD-L1		L/D	HLA-DR	CD24	IgM	CD45	CD20

Supplementary Figure 2. PD-1/TIM-3 co-expression by $CD8^+$ T cells (**A**) and $CD4^+$ T cells (**B**) based on clinical features.



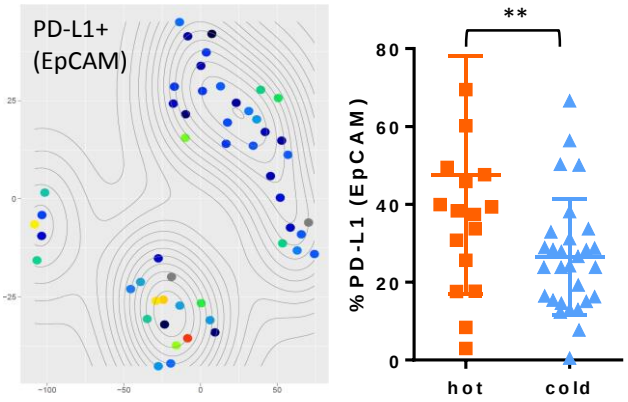
Supplementary Figure 3. Percent of PD-L1^{+} epithelial cells (EpCAM^{+}) detected by flow correlates with the percent of PD-L1 in tumor cells by IHC (**A**). Both correlate with "hot" and "cold" cluster breakdown (**B**).

A

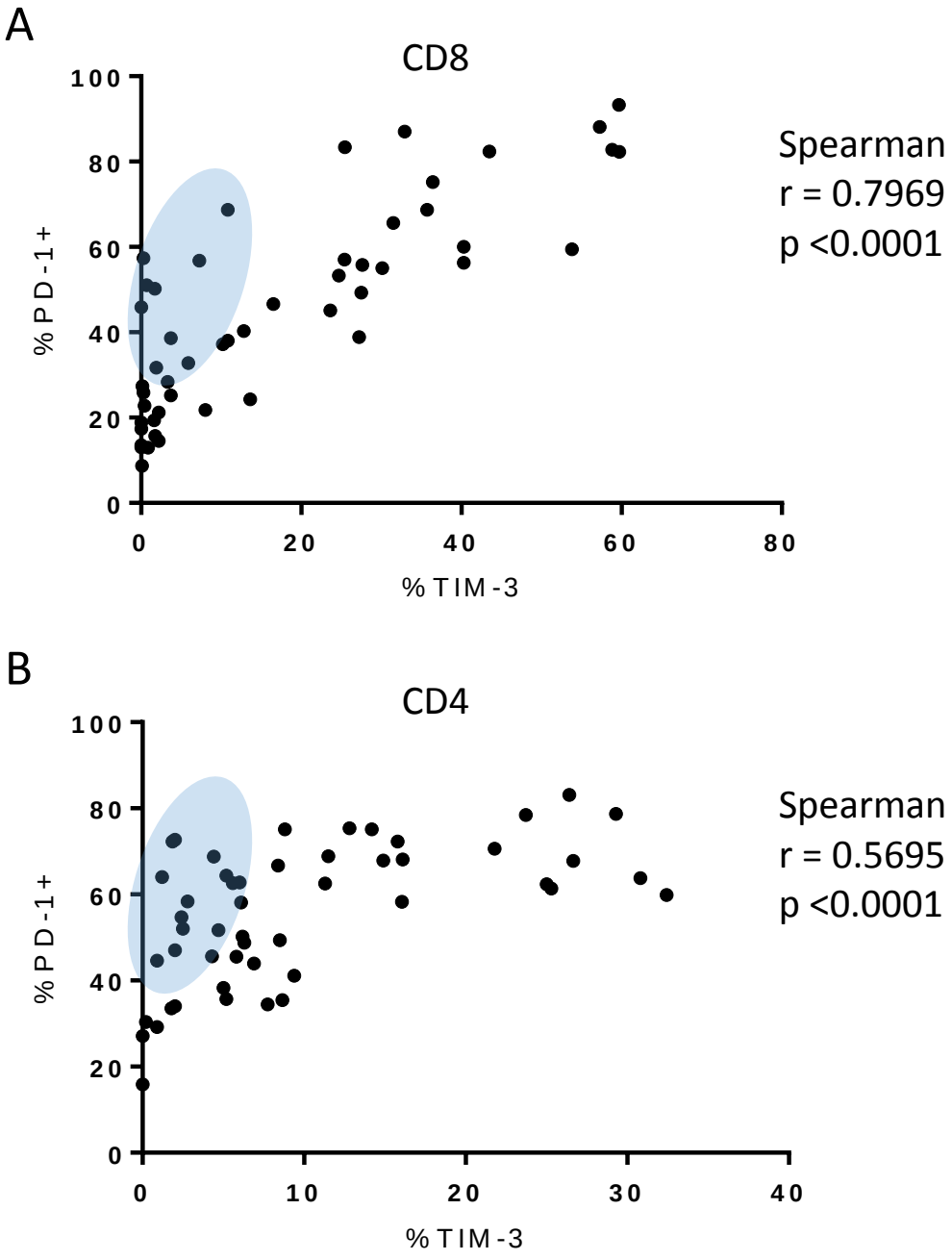


Spearman
r = 0.5225
p = 0.0005

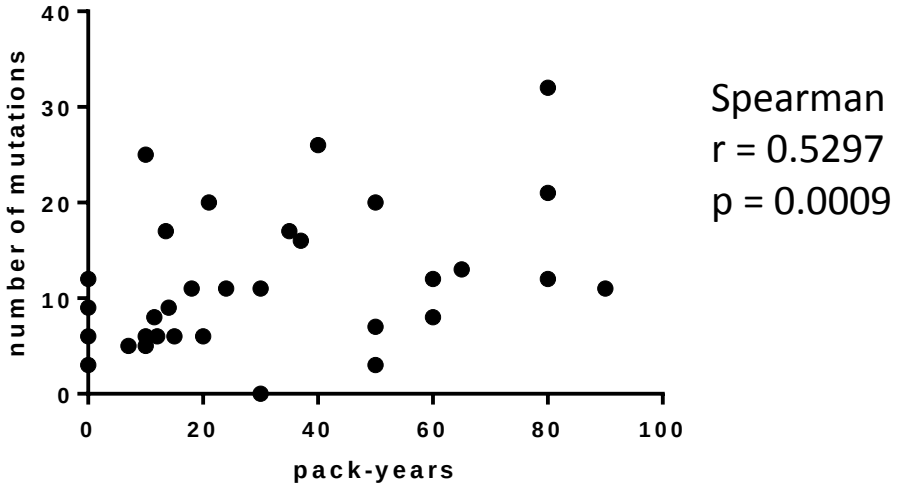
B



Supplementary Figure 4. Strong correlation between %PD-1 and %TIM-3 expression by both $CD8^+$ T cells (**A**) and $CD4^+$ T cells (**B**).

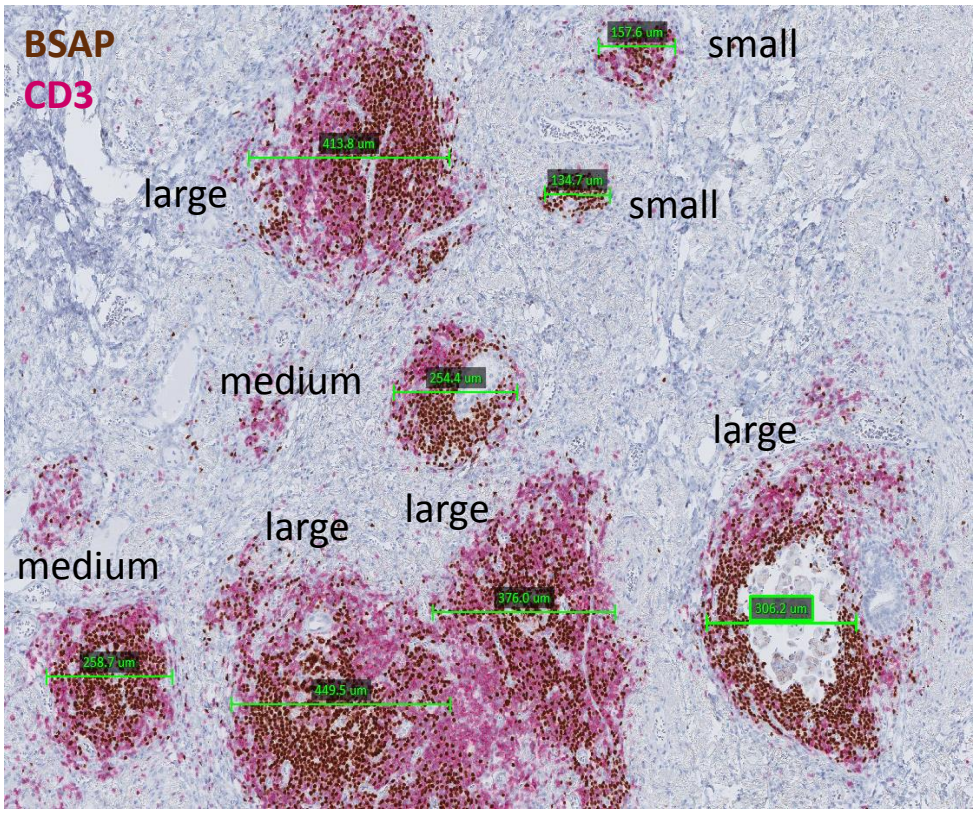


Supplementary Figure 5. Number of mutations detected by OncoPanel sequencing highly correlates with patient reported smoking status in pack-years.

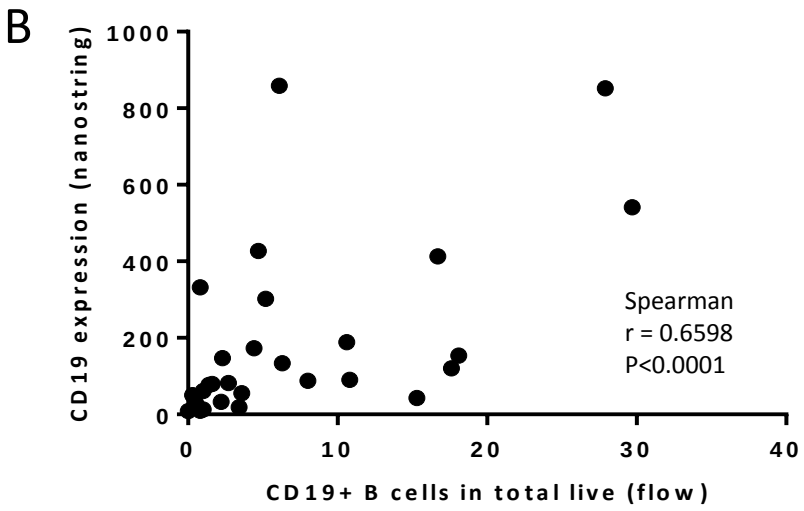


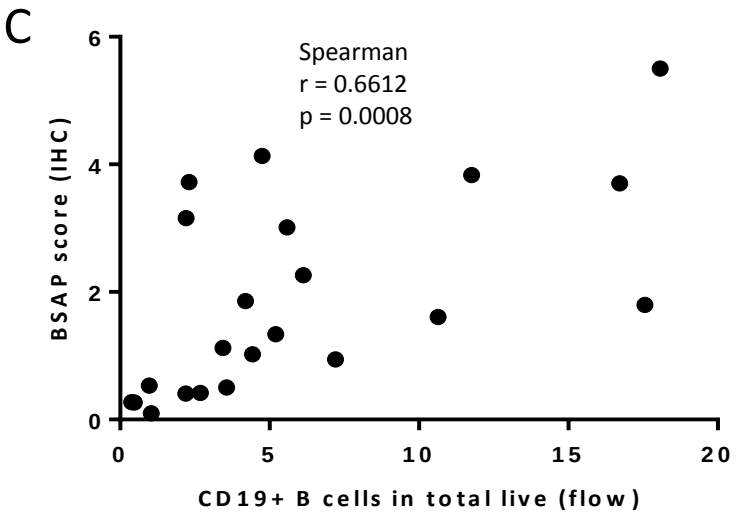
Supplementary Figure 6. Significantly differentially regulated genes by Nanostring in "hot" versus "cold" immnuophenotypic clusters.

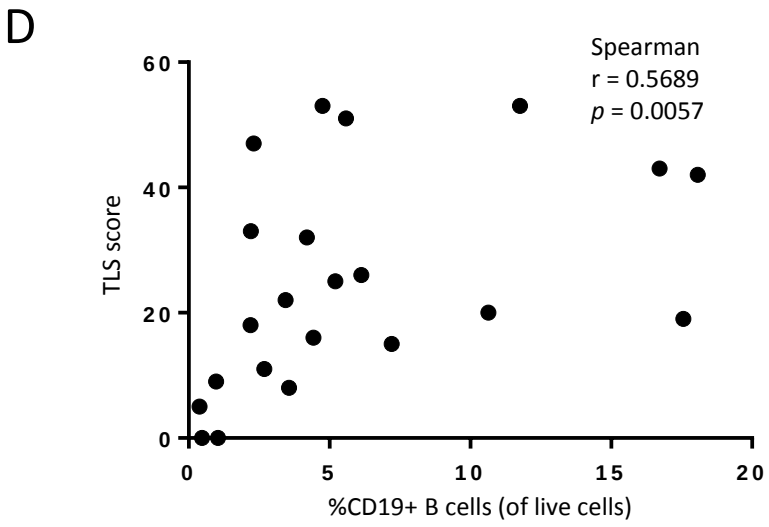
	Log2 fold change	Lower confidence limit	Upper confidence limit	P-value	FDR	Gene.sets
ADA	2.08	1.48	2.69	2.93E-07	0.000214	B-Cell Functions, T-Cell Functions
C4BPA	-4.45	-6.14	-2.76	2.04E-05	0.00538	Complement
GZMB	1.57	0.959	2.17	2.57E-05	0.00538	Cell Functions, Cytotoxicity
FOS	-2.38	-3.31	-1.45	2.95E-05	0.00538	
TNFSF4	1.41	0.845	1.97	3.81E-05	0.00556	Chemokines, TNF Superfamily
TOLLIP	-0.569	-0.807	-0.331	7.01E-05	0.00708	
C8B	-1.74	-2.47	-1.01	7.49E-05	0.00708	Complement
CXCL10	2.46	1.42	3.5	8.48E-05	0.00708	Chemokines, Cytokines, Pathogen Defense, Regulation, T-Cell Functions
CDK1	1.63	0.934	2.32	8.73E-05	0.00708	
CXCL9	2.49	1.41	3.57	0.000108	0.00785	Chemokines, Regulation, T-Cell Functions
VEGFC	1.54	0.855	2.23	0.000153	0.00977	
CREBBP	-0.859	-1.24	-0.475	0.000161	0.00977	
CXCL13	2.72	1.48	3.97	0.000213	0.0115	Chemokines
ITGA5	1.7	0.915	2.48	0.000228	0.0115	Adhesion
CTSH	-1.71	-2.5	-0.915	0.000247	0.0115	
BIRC5	1.51	0.805	2.21	0.000261	0.0115	Cell Cycle
FOXJ1	-3.43	-5.05	-1.82	0.000282	0.0115	
STAT1	1.36	0.723	2.01	0.000284	0.0115	Chemokines, Regulation
CCL17	-2.37	-3.5	-1.24	0.000318	0.0122	Chemokines
EGR1	-1.87	-2.78	-0.951	0.000444	0.0156	Senescence, T-Cell Functions
TNFSF15	-1.48	-2.2	-0.753	0.00045	0.0156	Chemokines, TNF Superfamily
PLA2G1B	-3.13	-4.68	-1.58	0.000482	0.016	Regulation
PRKCE	-0.759	-1.14	-0.381	0.000519	0.0165	Macrophage Functions
IL6R	-1.11	-1.66	-0.553	0.00055	0.0167	Cytokines
VCAM1	2.05	0.999	3.1	0.000705	0.0206	Adhesion, Regulation
TTK	1.37	0.656	2.08	0.000828	0.0232	
SIGIRR	-0.984	-1.5	-0.464	0.000951	0.0257	
CD1C	-1.55	-2.38	-0.723	0.00104	0.0271	T-Cell Functions
CCL8	1.51	0.702	2.32	0.00108	0.0272	Chemokines, Regulation
PBK	1.32	0.611	2.04	0.00113	0.0276	
ICAM4	-2.71	-4.18	-1.25	0.00118	0.0279	Adhesion, Regulation
STAT6	-1.07	-1.65	-0.488	0.00125	0.028	Chemokines, Regulation, T-Cell Functions
CCND3	-1.3	-2.01	-0.593	0.00127	0.028	Cell Cycle
C6	-2	-3.09	-0.899	0.00137	0.0281	Complement
NUP107	0.621	0.279	0.962	0.00138	0.0281	Cell Cycle
RORC	-2.32	-3.6	-1.05	0.00138	0.0281	Cell Functions
FCER1A	-1.98	-3.08	-0.884	0.00149	0.0294	
IL18	1.02	0.451	1.59	0.00157	0.0301	Interleukins, T-Cell Functions
PRG2	-1.16	-1.82	-0.497	0.00196	0.0367	Pathogen Defense
FCGR3A	1.27	0.538	2.01	0.00213	0.0389	Regulation
CCL23	-1.4	-2.21	-0.584	0.00231	0.041	Chemokines, Regulation
COL3A1	3.23	1.34	5.12	0.00236	0.041	Regulation
RRAD	-2	-3.17	-0.82	0.00255	0.0433	Cell Functions
REPS1	0.567	0.23	0.904	0.00275	0.0456	Cell Functions

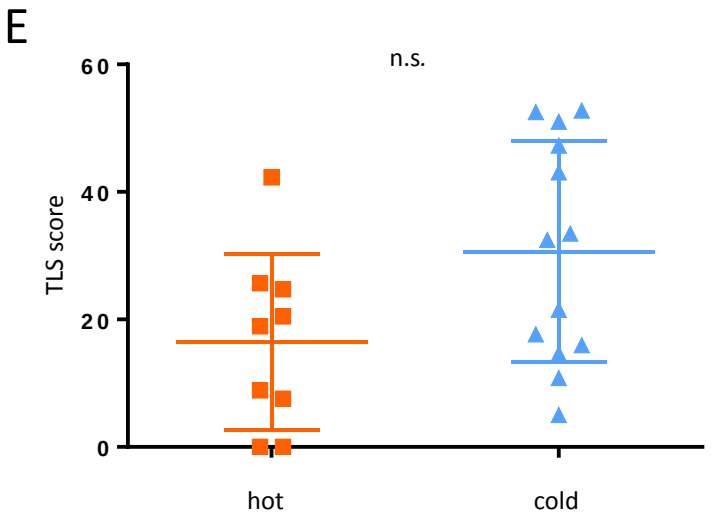


Supplementary Figure 7. TLS size was accessed for quantification (**A**). Percent of $CD19^+$ B cells defined by flow correlates with the Nanostring counts for CD19 gene expression (**B**) and B cell count by IHC (**C**). TLS score highly correlates with abundance of B cells quantified by flow (**D**) but not with "hot" or "cold" immunophenotype (**E**). Scale bars measuring TLS size to the tenth of a µm are overlayed onto image.



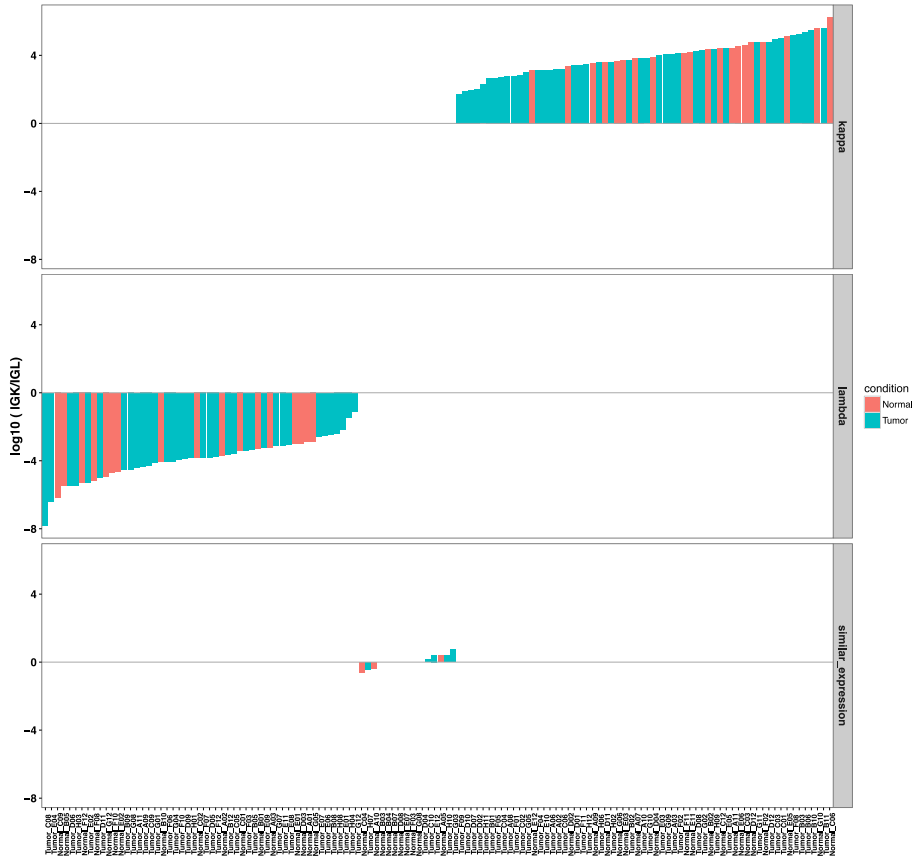


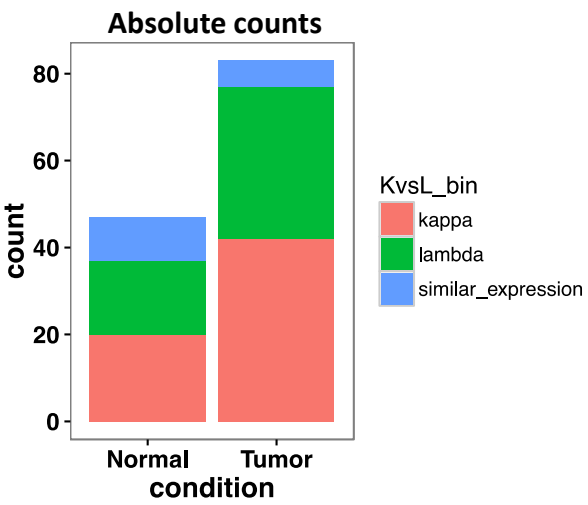


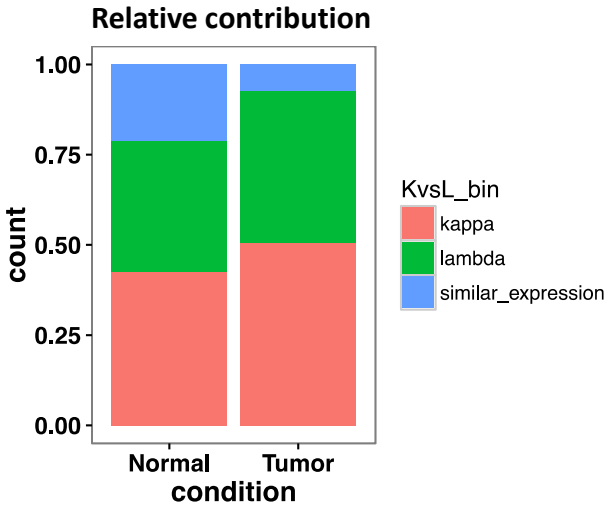


Supplementary Figure 8. No significant differences between Ig light chains between tumor B cells and normal lung B cells or between IL-10^{+} B cells and IL-10^{-} B cells.

	Normal	Tumor
kappa	20	42
lambda	17	35
similar_expression	10	6







Supplementary Figure 9. Immune parameters used for clustering in Figure 4.

	immune parameter
1	%EpCAM+ cells (live cells)
2	%CD45+ cells (live cells)
3	%CD3+ T cells (CD45+)
4	%CD19+ T cells (CD45+)
5	%CD56+ NK cells (CD45+)
6	%CD33+ monocytes (CD45+)
7	%CD66b+ granulocytes (CD45+)
8	%CD16+ NK cells
9	%CD8+ T cells (CD3+)
10	CD8/CD4 T cell ratio
11	%TIM-3+ (CD4+ T cells)
12	%PD-1+ (CD4+ T cells)
13	%TIM-3+ (CD8+ T cells)
14	%PD-1+ (CD8+ T cells)
15	%CD4+ T cells (CD3+)