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Supplementary information

SARS-CoV-2 mRNA vaccines sensitize tumours to immune checkpoint blockade

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Supplementary Information Guide

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6. Supplementary Table 3: Cox multivariable proportional hazards regression analysis of factors influencing overall survival non-small cell lung cancer patients. This multivariable analysis included the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 2** for descriptions of variables included in analysis. ++ Categories with fewer than 5 cases are reported for completeness but were considered not statistically meaningful due to convergence and insufficient data for reliable inference. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 unless otherwise noted.

7. Supplementary Table 4: Cox univariable proportional hazards regression analysis of factors influencing overall survival in unresectable Stage III non-small cell lung cancer patients. See **Supplementary Table 1** for descriptions of variables included in analysis. "Radiation prior to ICI" represents whether a patient received radiation in the 200 days before ICI, or not. ++ Categories with fewer than 5 cases are reported for completeness but were considered not statistically meaningful due to convergence and insufficient data for reliable inference. AKT and HER2/ERBB2 mutations did not occur in this subset of patients with Stage III UR NSCLC. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****<0.0001 unless otherwise noted **(Fig 1b).**

8. Supplementary Table 5: Cox multivariable proportional hazards regression analysis of factors influencing overall survival in unresectable Stage III non-small cell lung cancer patients. This multivariable analysis included the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 2** for descriptions of variables included in analysis. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****<0.0001 unless otherwise noted. **(Fig 1b).**

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9. **Supplementary Table 6: Cox univariable proportional hazards regression analysis of factors influencing overall survival in Stage IV non-small cell lung cancer patients.** "Brain/Liver Mets at ICI Start" describes whether or not a patient had brain or liver metastases at the beginning of their relevant ICI treatment. See **Supplementary Table 1** for descriptions of other variables included in analysis. ++ Categories with fewer than 5 cases are reported for completeness but were considered not statistically meaningful due to convergence and insufficient data for reliable inference. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 unless otherwise noted **(Fig 1c).**

10. **Supplementary Table 7: Cox multivariable proportional hazards regression analysis of factors influencing overall survival in Stage IV non-small cell lung cancer patients.** This multivariable analysis included the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 1 and 5** for descriptions of variables included in analysis. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ***p<0.001, **** p<.0001 unless otherwise noted. **(Fig 1c).**

11. **Supplementary Table 8: Cox univariable proportional hazards regression analysis of factors influencing overall survival in Stage IV melanoma patients receiving their first round of immunotherapy.** The majority of variables have the same definitions as reported in **Supplementary Table 2.** "NRAS" - "GNAQ" are binary descriptions of whether patients had known mutations in these genes at the time of tumor biopsy. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001 unless otherwise noted.

12. **Supplementary Table 9: Cox multivariable proportional hazards regression analysis of factors influencing overall survival in Stage IV melanoma patients receiving first-line immunotherapy.** This multivariable analysis includes the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 8** for descriptions of variables included in analysis. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001 unless otherwise noted.

13. **Supplementary Table 10: Cox univariable proportional hazards regression analysis of factors influencing progression-free survival in Stage IV melanoma patients receiving their first round of immunotherapy.** See **Supplementary Table 8** for descriptions of variables included in analysis. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001 unless otherwise noted.

14. **Supplementary Table 11: Cox multivariable proportional hazards regression analysis of factors influencing progression-free survival in Stage IV melanoma patients receiving their first round of immunotherapy.** This multivariable analysis included the factors in the univariable analysis that had a significant relationship with progression-free survival alone in the patient population. See **Supplementary Table 8** for descriptions of variables included in analysis. *p<0.05, **p<0.01, ***p<0.001 unless otherwise noted. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values.

15. **Supplementary Table 12: Antibodies utilized in myeloid panels for murine experiments. (Fig 2f-o, Extended Data Fig. 9a-c).**

16. **Supplementary Table 13: Antibody panel for murine T cell markers.**

17. **Supplementary Table 14: Antibody panel for AIM assay.**

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a

NSCLC Demographics		No Vaccine	Vaccine <100 Days
n =		704	180
Interval from COVID-mRNA vaccine, days		No vaccine	0-100
Gender			
	Male, %	354 (50.3%)	88 (48.9%)
Age at ICI start, median, range		64.0 (26 – 89+)	65.7 (30.7 – 89+)
Ethnicity			
	Asian	46 (6.5%)	9 (5.0%)
	Black	55 (7.8%)	17 (9.4%)
	Caucasian	569 (80.8%)	147 (81.7%)
	American Indian/Alaskan Native	6 (0.9%)	1 (0.6%)
	Native Hawaiian/Pacific Islander	1 (0.1%)	0 (0%)
	Unknown	5 (0.7%)	3 (1.7%)
	Other	22 (3.1%)	3 (1.7%)
Clinical Stage			
	IIIa	68 (9.7%)	24 (13.3%)
	IIIb	57 (8.1%)	10 (5.6%)
	IIIc	5 (0.1%)	6 (3.33%)
	IV	574 (81.5%)	140 (77.8%)
Mutations			
	AKT	1 (0.1%)	3 (1.7%)
	EGFR	128 (18.2%)	30 (16.7%)
	HER2/ERBB2	8 (1.1%)	3 (1.7%)
	BRAF	39 (5.5%)	9 (5.0%)
	KRAS	200 (28.4%)	60 (33.3%)
	ALK	19 (2.7%)	2 (1.1%)
	PIK3CA	60 (8.5%)	14 (7.8%)
	MET	102 (14.5%)	17 (9.4%)
	CDKN2A	42 (6.0%)	11 (6.1%)
	STK11	83 (11.8%)	22 (12.2%)
	P53	340 (48.3%)	77 (42.8%)
	NF	68 (9.7%)	16 (8.9%)
	RET	18 (2.6%)	0 (0.0%)
	ROS1	11 (1.6%)	5 (2.8%)
ICI Agent			
	Atezolizumab	43 (6.1%)	9 (5.0%)
	Durvalumab	80 (11.4%)	30 (16.7%)
	Nivolumab	73 (10.4%)	5 (2.8%)
	Nivolumab/Ipi	60 (8.5%)	13 (7.2%)
	Pembrolizumab	448 (63.6%)	122 (67.8%)
	Pembrolizumab/Ipi	0 (0.0%)	1 (0.6%)
Histology			
	Adenocarcinoma	614 (87.2%)	158 (87.8%)
	Squamous Cell Carcinoma	71 (10.1%)	18 (10.0%)
	Other	19 (2.7%)	4 (2.2%)

b

Stage IV Melanoma Demographics		No Vaccine	Vaccine <100 Days
n =		167	43
Interval from COVID-mRNA vaccine, days		No vaccine	0-100
Gender			
	Male, %	109 (65.3%)	30 (69.8%)
Age at ICI start, median, range		63.5 (26.2 – 89+)	68.9 (22.9 - 84.5)
Ethnicity			
	White	149 (89.2%)	40 (93.0%)
	Black	3 (1.8%)	0 (0.0%)
	Asian	2 (1.2%)	0 (0.0%)
	Hispanic	6 (3.6%)	3 (7.0%)
	Unknown	6 (3.6%)	0% (0.0%)
	Other	1 (0.6%)	0% (0.0%)
Mutations			
	NRAS	34 (20.4%)	9 (20.9%)
	BRAF	64 (38.3%)	15 (34.9%)
	KIT	15 (9.0%)	5 (11.6%)
	PTEN	16 (9.6%)	2 (4.7%)
	GNA11	2 (1.2%)	2 (4.7%)
	GNAQ	2 (1.2%)	1 (2.3%)
ICI Drug			
	Avelumab	1 (0.6%)	0 (0.0%)
	Ipilimumab	1 (0.6%)	0 (0.0%)
	Ipilimumab/Nivolumab	80 (47.9%)	19 (44.2%)
	Nivolumab	61 (36.5%)	14 (32.6%)
	Pembrolizumab	20 (12.0%)	8 (18.6%)
	Pembrolizumab/Ipi	4 (2.4%)	2 (4.7%)

Supplementary Table 1: Demographics for patients with NSCLC (a) (Fig 1a-c) or Stage IV Melanoma (b) (Fig 1d–e).

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (reference: No mRNA Vaccination ever)	-0.6324	0.1366	0.5313	0.4065	0.6944	3.63E-6	****
Ethnicity American Indian/Alaskan Native (Reference: White)	0.2774	0.5030	1.3196	0.4923	3.5370	0.5814	ns
Ethnicity Asian (Reference: White)	0.2327	0.1815	1.2620	0.8842	1.8012	0.1999	ns
Ethnicity Black (Reference: White)	0.1916	0.1609	1.2111	0.8835	1.6603	0.2339	ns
Ethnicity Native Hawaiian/Pacific Islander (Reference: White) ++	-11.9653	1143.5840	0.0000	0.0000	Inf	0.9917	ns
Ethnicity Other (Reference: White)	0.4646	0.2414	1.5915	0.9915	2.5544	0.0543	ns
Ethnicity Unknown (Reference: White)	-0.5356	0.5798	0.5853	0.1879	1.8237	0.3557	ns
Histology Other (reference: Adenocarcinoma)	-0.1513	0.3054	0.8596	0.4723	1.5642	0.6204	ns
Histology Squamous (reference: Adenocarcinoma)	-0.0460	0.1568	0.9551	0.7024	1.2986	0.7693	ns
Steroid use within 1 month of ICI Start	0.3376	0.1186	1.4015	1.1108	1.7683	0.0044	**
Steroid use within 1 month of Vaccination	0.6767	0.3470	1.9674	0.9965	3.8841	0.0512	ns
Age at ICI Start	0.0028	0.0042	1.0028	0.9946	1.0112	0.5019	ns
ECOG	0.4395	0.0585	1.5520	1.3840	1.7404	5.53E-14	****
PDL1 (TPS)	-0.0054	0.0014	0.9946	0.9920	0.9973	7.22E-5	***
Line of Immunotherapy Treatment	-0.1726	0.1241	0.8415	0.6597	1.0733	0.1644	ns
EGFR	0.2139	0.1132	1.2385	0.9921	1.5461	0.0587	ns
KRAS	0.1969	0.0966	1.2176	1.0075	1.4715	0.0417	*
HER2ERBB2	-0.0564	0.4498	0.9452	0.3914	2.2823	0.9003	ns
BRAF	-0.2528	0.2096	0.7766	0.5150	1.1713	0.2279	ns
AKT	-0.1137	0.7088	0.8925	0.2225	3.5802	0.8725	ns
ALK	0.3291	0.2714	1.3897	0.8164	2.3654	0.2253	ns
MET	0.1712	0.1244	1.1868	0.9299	1.5145	0.1688	ns
STK11	0.6580	0.1261	1.9309	1.5080	2.4725	1.83E-7	****
ROS1	-0.1977	0.3566	0.8206	0.4079	1.6508	0.5793	ns
PIK3CA	0.0685	0.1599	1.0709	0.7828	1.4650	0.6685	ns
CDKN2A	0.2217	0.1780	1.2481	0.8805	1.7693	0.2131	ns
P53	0.1384	0.0912	1.1484	0.9604	1.3732	0.1292	ns
NF	0.2767	0.1403	1.3187	1.0017	1.7360	0.0486	*
RET	0.6564	0.2715	1.9279	1.1324	3.2820	0.0156	*
Stage IIIb (reference: IIIa)	-0.0696	0.2636	0.9327	0.5564	1.5635	0.7916	ns
Stage IIIc (reference: IIIa)	0.0230	0.5287	1.0233	0.3630	2.8844	0.9653	ns
Stage IV (reference: IIIa)	0.7305	0.1785	2.0761	1.4634	2.9454	4.25E-5	****
English as Primary Language (Reference: No)	-0.0581	0.2285	0.9436	0.6030	1.4766	0.7993	ns
Heart Disease	-0.1171	0.0913	0.8895	0.7437	1.0638	0.1997	ns
Respiratory Condition	0.5354	0.1215	1.7081	1.3460	2.1675	1.06E-5	****
Immune Deficiency	-0.0415	0.1551	0.9594	0.7078	1.3002	0.7891	ns
Diabetes	0.1742	0.1075	1.1903	0.9642	1.4695	0.1050	ns
CKD	-0.0543	0.1294	0.9471	0.7350	1.2205	0.6747	ns
Liver Failure	0.2652	0.3568	1.3037	0.6479	2.6235	0.4572	ns
CNS Disease	-0.8233	0.7087	0.4390	0.1094	1.7607	0.2453	ns
Concurrent Chemotherapy during ICI	0.2532	0.0917	1.2881	1.0761	1.5418	0.0058	**
Immunotherapy Agent Atezolizumab (Reference: Pembrolizumab)	-0.0605	0.1973	0.9413	0.6394	1.3858	0.7593	ns
Immunotherapy Agent Durvalumab (Reference: Pembrolizumab)	-0.6195	0.1681	0.5382	0.3872	0.7482	0.0002	***
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.2199	0.1403	1.2459	0.9464	1.6402	0.1170	ns
Immunotherapy Agent Nivolumab + Ipilimumab (Reference: Pembrolizumab)	-0.0201	0.1627	0.9801	0.7124	1.3483	0.9015	ns
Immunotherapy Agent Pembrolizumab + Ipilimumab (Reference: Pembrolizumab) ++	-13.0705	772.5062	0.0000	0.0000	Inf	0.9865	ns
BMI	0.0076	0.0116	1.0076	0.9850	1.0308	0.5124	ns
Gender (Reference: Female)	0.1582	0.0910	1.1714	0.9801	1.4001	0.0821	ns
Previous history of malignancy at ICI Start	-0.0561	0.2714	0.9455	0.5555	1.6093	0.8364	ns
Previous cycles of systemic therapy	0.0951	0.0385	1.0997	1.0199	1.1859	0.0135	*
Treatment Year	-0.0845	0.0275	0.9190	0.8707	0.9699	0.0022	**

Supplementary Table 2: **Cox univariable proportional hazards regression analysis of factors influencing overall survival in non-small cell lung cancer patients.** "COVID mRNA Vaccine" is defined as the receipt of a COVID mRNA vaccination within 100 days of the initiation of immune checkpoint inhibition (ICI). "PDL1" describes tumor proportion score at time of primary tumor biopsy. "Steroid use within 1 month of ICI start" and "Steroid use within 1 month of vaccination" indicate whether a patient received a systemic steroid within 1 month before or after immunotherapy start date/vaccination or not. "Cycle of immunotherapy" was numeric and established which cycle of immunotherapy the patient received. "Previous Cycles of Systemic Therapy" is numeric and describes the quantity of past chemotherapies/other systemic therapies. "EGFR" - "RET" are binary descriptions of whether patients had known mutations in these genes at the time of tumor biopsy. Performance status quantified by the Eastern Cooperative Oncology Group performance status scale ("ECOG"), "Age at ICI start", "BMI", and "Treatment Year" were defined as numerical/continuous variables. Comorbidities (heart disease, immunodeficiency, diabetes, history of other malignancy, etc.) represent patient characteristics at the start of ICI. "Sex," "Ethnicity," and "Histology" (Adenocarcinoma, Squamous Cell, and Other) were described as categorical variables. "Immunotherapy Agent" is a categorical variable. Clinical stage was also defined as a categorical variable. ++ Categories with fewer than 5 cases are reported for completeness but were considered not statistically meaningful due to convergence and insufficient data for reliable inference. For all analyses, "Steroid use within 1 month of Vaccination" was only considered for patients with COVID mRNA vaccination within 100 days of ICI start, n = 180 for NSCLC and n = 43 for Melanoma. This was applicable for all Supplementary Figures. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 unless otherwise noted. **(Fig 1a).**

Variable	Beta	St. Error	adj HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (reference: No mRNA Vaccination ever)	-0.6689	0.1671	0.5123	0.3692	0.7107	6.24E-5	****
Steroid use within 1 month of ICI Start	0.3289	0.1224	1.3895	1.0931	1.7663	0.0072	**
ECOG	0.4291	0.0615	1.5358	1.3614	1.7326	3.06E-12	****
PDL1	-0.0047	0.0016	0.9953	0.9923	0.9983	0.0025	**
KRAS	0.0308	0.1062	1.0313	0.8375	1.2700	0.7716	ns
STK11	0.4524	0.1419	1.5720	1.1904	2.0760	0.0014	**
Stage IIIb (reference: IIIa)	-0.0020	0.2782	0.9980	0.5785	1.7217	0.9942	ns
Stage IIIc (reference: IIIa)	0.3138	0.5379	1.3687	0.4770	3.9275	0.5596	ns
Stage IV (reference: IIIa)	0.7516	0.2265	2.1204	1.3604	3.3051	0.0009	***
NF	0.1835	0.1461	1.2014	0.9022	1.5999	0.2093	ns
RET	0.6024	0.2816	1.8265	1.0517	3.1721	0.0324	*
Respiratory Condition	0.3773	0.1265	1.4584	1.1381	1.8689	0.0029	**
Concurrent Chemotherapy during ICI	0.1858	0.1261	1.2042	0.9405	1.5419	0.1406	ns
Immunotherapy Agent Atezolizumab (Reference: Pembrolizumab)	-0.0345	0.2072	0.9661	0.6436	1.4500	0.8676	ns
Immunotherapy Agent Durvalumab (Reference: Pembrolizumab)	0.0563	0.2437	1.0579	0.6562	1.7056	0.8173	ns
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.1373	0.1745	1.1472	0.8148	1.6150	0.4315	ns
Immunotherapy Agent Nivolumab + Ipilimumab (Reference: Pembrolizumab)	0.0069	0.1986	1.0070	0.6822	1.4863	0.9721	ns
Immunotherapy Agent Pembrolizumab + Ipilimumab (Reference: Pembrolizumab) ++	-12.5047	826.3909	0.0000	0.0000	Inf	0.9879	ns
Previous cycles of systemic therapy	0.1184	0.0412	1.1256	1.0383	1.2204	0.0041	**
Treatment Year	0.0335	0.0387	1.0341	0.9586	1.1156	0.3862	ns

Supplementary Table 3: **Cox multivariable proportional hazards regression analysis of factors influencing overall survival non-small cell lung cancer patients.** This multivariable analysis included the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 2** for descriptions of variables included in analysis. ++ Categories with fewer than 5 cases are reported for completeness but were considered not statistically meaningful due to convergence and insufficient data for reliable inference. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 unless otherwise noted. **(Fig 1a).**

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (reference: No mRNA Vaccination ever)	-0.8576	0.4332	0.4242	0.1815	0.9916	0.0478	*
Stage IIIb (reference: IIIa)	-0.0026	0.2767	0.9974	0.5799	1.7154	0.9925	ns
Stage IIIc (reference: IIIa)	0.0094	0.5340	1.0095	0.3545	2.8748	0.9859	ns
Ethnicity American Indian/Alaskan Native (Reference: White)	0.4534	1.0122	1.5737	0.2164	11.4425	0.6542	ns
Ethnicity Asian (Reference: White) ++	-17.5951	4101.6438	0.0000	0.0000	Inf	0.9966	ns
Ethnicity Black (Reference: White)	-0.0862	0.4328	0.9174	0.3928	2.1426	0.8421	ns
Ethnicity Other (Reference: White)	1.6501	1.0249	5.2075	0.6986	38.8185	0.1074	ns
Ethnicity Unknown (Reference: White) ++	-17.5987	7618.3177	0.0000	0.0000	Inf	0.9982	ns
Histology Other (reference: Adenocarcinoma)	0.0765	0.5387	1.0795	0.3756	3.103	0.8870	ns
Histology Squamous (reference: Adenocarcinoma)	0.8564	0.2781	2.3547	1.3654	4.0609	0.0021	**
Steroid within 1 month of ICI	0.3737	0.3488	1.4531	0.7335	2.8789	0.2840	ns
Steroid within 1 month of Vaccination	1.3536	1.098	3.8713	0.4495	33.3426	0.2179	ns
Age at ICI Start	0.0193	0.0144	1.0195	0.9912	1.0486	0.1787	ns
ECOG	0.3625	0.1620	1.4369	1.0460	1.9738	0.0253	*
PDL1 (TPS)	-0.0035	0.0038	0.9965	0.9891	1.0039	0.3475	ns
Line of Immunotherapy	-0.6079	0.8579	0.5445	0.1013	2.9259	0.4786	ns
EGFR	-0.2963	0.4695	0.7436	0.2963	1.8663	0.5280	ns
KRAS	0.0606	0.3359	1.0625	0.5501	2.0524	0.8568	ns
BRAF	-0.1683	0.7208	0.8451	0.2058	3.4712	0.8154	ns
ALK ++	-15.0160	3102.4518	0.0000	0.0000	Inf	0.9961	ns
MET	-0.3924	0.5944	0.6754	0.2107	2.1653	0.5091	ns
STK11	0.6333	0.5958	1.8838	0.5860	6.0560	0.2878	ns
ROS1 ++	-17.0430	4276.9672	0.0000	0.0000	Inf	0.9968	ns
PIK3CA	-0.1203	0.5220	0.8867	0.3188	2.4665	0.8178	ns
CDKN2A	1.0812	0.4328	2.9481	1.2621	6.8863	0.0125	*
P53	-0.0959	0.2661	0.9086	0.5394	1.5305	0.7186	ns
NF	0.3318	0.4320	1.3935	0.5976	3.2495	0.4424	ns
RET	0.3773	0.7214	1.4584	0.3547	5.9970	0.6009	ns
Radiation prior to ICI	-0.0086	0.2748	0.9914	0.5785	1.6989	0.9749	ns
English as Primary Language (Reference: No) ++	17.0490	3925.4429	25368624.1974	0.0000	Inf	0.9965	ns
Heart Disease	-0.0608	0.2661	0.9410	0.5585	1.5853	0.8192	ns
Respiratory Condition	0.5730	0.3368	1.7736	0.9166	3.4319	0.0889	ns
Immune Deficiency	0.1002	0.4040	1.1054	0.5008	2.4401	0.8041	ns
Diabetes	0.4835	0.3018	1.6217	0.8975	2.9301	0.1092	ns
CKD	-0.2112	0.3821	0.8096	0.3829	1.7120	0.5804	ns
Liver Failure	0.7460	1.0152	2.1086	0.2883	15.4227	0.4625	ns
CNS Disease ++	-16.0211	3783.1244	0.0000	0.0000	Inf	0.9966	ns
Concurrent Chemotherapy during ICI	0.2495	0.3160	1.2833	0.6908	2.3840	0.4299	ns
Immunotherapy Agent Atezolizumab (Reference: Pembrolizumab)	0.1238	0.5213	1.1318	0.4075	3.1438	0.8123	ns
Immunotherapy Agent Durvalumab (Reference: Pembrolizumab)	-0.2283	0.3240	0.7959	0.4217	1.5019	0.4810	ns
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.5384	0.4633	1.7132	0.6910	4.2475	0.2452	ns
Immunotherapy Agent Nivolumab + Ipilimumab (Reference: Pembrolizumab)	-1.0266	1.0359	0.3582	0.0470	2.7282	0.3217	ns
BMI	-0.0259	0.0376	0.9744	0.9051	1.0490	0.4908	ns
Gender (Reference: Female)	0.1366	0.2664	1.1464	0.6801	1.9324	0.6081	ns
Previous history of malignancy at ICI Start	-0.2318	0.5936	0.7931	0.2478	2.5385	0.6961	ns
Previous cycles of systemic therapy	0.2040	0.1521	1.2263	0.9102	1.6521	0.1798	ns
Treatment Year	-0.0903	0.0865	0.9136	0.7712	1.0823	0.2962	ns

Supplementary Table 4: **Cox univariable proportional hazards regression analysis of factors influencing overall survival in unresectable Stage III non-small cell lung cancer patients.** See **Supplementary Table 2** for descriptions of variables included in analysis. "Radiation prior to ICI" represents whether a patient received radiation in the 200 days before ICI, or not. ++ Categories with fewer than 5 cases are reported for completeness but were considered not statistically meaningful due to convergence and insufficient data for reliable inference. AKT and HER2/ERBB2 mutations did not occur in this subset of patients with Stage III Unresectable NSCLC. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****<0.0001 unless otherwise noted **(Fig 1b).**

Variable	Beta	St. Error	adj HR	2.5% CI	97.5% CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (reference: No mRNA Vaccination ever)	-0.9860	0.4453	0.3731	0.1559	0.8930	0.0268	*
Histology Other (reference: Adenocarcinoma)	0.1067	0.6185	1.1126	0.3310	3.7396	0.8630	ns
Histology Squamous (reference: Adenocarcinoma)	0.8644	0.2929	2.3736	1.3370	4.2141	0.0032	**
ECOG	0.3611	0.1838	1.4349	1.0009	2.0571	0.0494	*
CDKN2A	1.0148	0.4455	2.7589	1.1521	6.6067	0.0227	*

Supplementary Table 5: **Cox multivariable proportional hazards regression analysis of factors influencing overall survival in unresectable Stage III non-small cell lung cancer patients.** This multivariable analysis included the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 2** for descriptions of variables included in analysis. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****<0.0001 unless otherwise noted. **(Fig 1b).**

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (reference: No mRNA Vaccination ever)	-0.6063	0.1463	0.5454	0.4094	0.7265	3.41E-05	****
Ethnicity American Indian/Alaskan Native (Reference: White)	0.1883	0.5806	1.2072	0.3869	3.7670	0.7457	ns
Ethnicity Asian (Reference: White)	0.3336	0.1830	1.3961	0.9752	1.9985	0.0683	ns
Ethnicity Black (Reference: White)	0.2169	0.1737	1.2423	0.8839	1.7460	0.2116	ns
Ethnicity Native Hawaiian/Pacific Islander (Reference: White) ++	-11.9551	1045.5698	0.0000	0.0000	Inf	0.9909	ns
Ethnicity Other (Reference: White)	0.3157	0.2490	1.3712	0.8417	2.2336	0.2048	ns
Ethnicity Unknown (Reference: White)	-0.2291	0.5811	0.7953	0.2546	2.4838	0.6934	ns
Histology Other (reference: Adenocarcinoma)	0.4205	0.3824	1.5226	0.7196	3.2220	0.2716	ns
Histology Squamous (reference: Adenocarcinoma)	0.3814	0.2480	1.4644	0.9007	2.3807	0.1240	ns
Brain Mets at ICI Start	0.2543	0.1333	1.2896	0.9931	1.6745	0.0564	ns
Liver Mets at ICI Start	0.0812	0.1816	1.0845	0.7598	1.5481	0.6548	ns
Steroid within 1 month of ICI	0.3209	0.1270	1.3784	1.0746	1.7681	0.0115	*
Steroid within 1 month of Vaccination	0.4016	0.3850	1.4941	0.7026	3.1774	0.2969	ns
Age at ICI Start	0.0026	0.0044	1.0026	0.9939	1.0113	0.5620	ns
ECOG	0.4549	0.0640	1.5761	1.3903	1.7867	1.17E-12	****
PDL1 (TPS)	-0.0059	0.0015	0.9941	0.9912	0.9969	4.88E-05	****
Line of Immunotherapy	-0.1969	0.1243	0.8213	0.6437	1.0478	0.1131	ns
EGFR	0.1504	0.1185	1.1623	0.9214	1.4661	0.2044	ns
KRAS	0.1165	0.1023	1.1236	0.9195	1.3729	0.2547	ns
HER2ERBB2	-0.1790	0.4502	0.8361	0.3460	2.0205	0.6910	ns
BRAF	-0.2258	0.2193	0.7979	0.5192	1.2263	0.3032	ns
ALK	0.2453	0.2720	1.2781	0.7500	2.1779	0.3670	ns
MET	0.1378	0.1289	1.1477	0.8915	1.4776	0.2850	ns
STK11	0.5429	0.1307	1.7209	1.3321	2.2232	3.26E-5	****
ROS1	-0.0989	0.3573	0.9058	0.4497	1.8248	0.7820	ns
PIK3CA	0.1528	0.1681	1.1651	0.8380	1.6200	0.3634	ns
CDKN2A	0.1058	0.1959	1.1116	0.7572	1.6319	0.5892	ns
P53	0.1611	0.0978	1.1748	0.9698	1.4232	0.0996	ns
NF	0.3283	0.1497	1.3886	1.0356	1.8620	0.0283	*
RET	0.6874	0.2934	1.9886	1.1190	3.5338	0.0191	*
AKT	0.1534	0.7091	1.1658	0.2904	4.6792	0.8288	ns
English as Primary Language (Reference: No)	-0.2333	0.2295	0.7919	0.5050	1.2418	0.3094	ns
Heart Disease	-0.0613	0.0980	0.9405	0.7761	1.1397	0.5315	ns
Respiratory Condition	0.5368	0.1313	1.7105	1.3224	2.2125	4.35E-05	****
Immune Deficiency	-0.0144	0.1684	0.9857	0.7086	1.3711	0.9318	ns
Diabetes	0.1348	0.1158	1.1443	0.9119	1.4360	0.2446	ns
CKD	-0.0602	0.1389	0.9416	0.7171	1.2362	0.6647	ns
Liver Failure	0.1504	0.3814	1.1623	0.5504	2.4547	0.6933	ns
CNS Disease	-0.7091	0.7090	0.4921	0.1226	1.9750	0.3173	ns
Concurrent Chemotherapy during ICI	0.1223	0.0995	1.1301	0.9299	1.3734	0.2189	ns
Immunotherapy Agent Atezolizumab (Reference: Pembrolizumab)	0.0275	0.2260	1.0279	0.6601	1.6006	0.9032	ns
Immunotherapy Agent Durvalumab (Reference: Pembrolizumab)	0.1894	0.3385	1.2086	0.6225	2.3466	0.5757	ns
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.2472	0.1496	1.2805	0.9551	1.7168	0.0984	ns
Immunotherapy Agent Nivolumab + Ipilimumab (Reference: Pembrolizumab)	0.0011	0.1650	1.0011	0.7246	1.3833	0.9945	ns
Immunotherapy Agent Pembrolizumab + Ipilimumab (Reference: Pembrolizumab) ++	-13.9764	1201.6163	0.0000	0.0000	Inf	0.9907	ns
BMI	0.0163	0.0121	1.0165	0.9927	1.0408	0.1753	ns
Gender Male (Reference: Female)	0.1806	0.0976	1.1979	0.9894	1.4504	0.0641	ns
Previous history of malignancy at ICI Start	0.2574	0.3058	1.2935	0.7104	2.3554	0.4000	ns
Previous cycles of systemic therapy	0.0870	0.0385	1.0909	1.0115	1.1764	0.0240	*
Treatment Year	-0.0644	0.0293	0.9377	0.8853	0.9931	0.0280	*

Supplementary Table 6: Cox univariable proportional hazards regression analysis of factors influencing overall survival in Stage IV non-small cell lung cancer patients. "Brain/Liver Mets at ICI Start" describes whether or not a patient had brain or liver metastases at the beginning of their relevant ICI treatment. See **Supplementary Table 2** for descriptions of other variables included in analysis. ++ Categories with fewer than 5 cases are reported for completeness but were considered not statistically meaningful due to convergence and insufficient data for reliable inference. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 unless otherwise noted **(Fig 1c).**

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (reference: No mRNA Vaccination ever)	-0.6496	0.1770	0.5223	0.3692	0.7389	0.0002	***
Steroid within 1 month of ICI	0.3229	0.1311	1.3811	1.0681	1.7857	0.0138	*
ECOG at ICI Start	0.4228	0.0658	1.5263	1.3415	1.7365	1.34E-10	****
PDL1	-0.0055	0.0016	0.9945	0.9915	0.9975	0.0004	***
STK11	0.4428	0.1381	1.5570	1.1877	2.0412	0.0013	**
NF	0.1786	0.1563	1.1956	0.8802	1.6240	0.2529	ns
RET	0.5111	0.2973	1.6672	0.9310	2.9854	0.0855	ns
Respiratory Condition	0.3460	0.1366	1.4133	1.0813	1.8473	0.0113	*
Previous cycles of systemic therapy	0.1003	0.0406	1.1054	1.0210	1.1969	0.0135	*
Treatment Year	0.0386	0.0386	1.0394	0.9637	1.1210	0.3169	ns

Supplementary Table 7: **Cox multivariable proportional hazards regression analysis of factors influencing overall survival in Stage IV non-small cell lung cancer patients.** This multivariable analysis included the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 2 and 6** for descriptions of variables included in analysis. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001, ***p<0.001, **** p<.0001 unless otherwise noted. **(Fig 1c).**

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (relative to No mRNA Vaccination ever)	-0.8426	0.3016	0.4306	0.2384	0.7777	0.0052	**
Brain Metastasis at ICI Start	0.4207	0.2304	1.5230	0.9695	2.3924	0.0679	ns
Liver Metastasis at ICI Start	0.7483	0.2240	2.1135	1.3626	3.2781	0.0008	***
Steroid use within 1 month of Vaccination	-0.5927	0.7693	0.5528	0.1223	2.4971	0.4411	ns
Steroid use within 1 month of ICI Initiation	0.6556	0.2496	1.9262	1.1809	3.1420	0.0086	**
Age at ICI Initiation	0.0336	0.0086	1.0342	1.0169	1.0518	9.47E-5	***
NRAS	-0.1087	0.2637	0.8970	0.5350	1.5040	0.6801	ns
BRAF	-0.5670	0.2307	0.5673	0.3609	0.8915	0.0140	*
KIT	0.4321	0.3222	1.5405	0.8192	2.8969	0.1799	ns
PTEN	0.5299	0.3357	1.6987	0.8798	3.2796	0.1144	ns
GNA11	0.6313	0.5878	1.8801	0.5941	5.9502	0.2828	ns
GNAQ	1.7676	0.5967	5.8570	1.8188	18.8612	0.0031	**
ECOG	0.5401	0.1572	1.7162	1.2611	2.3355	0.0006	***
Gender Male (reference: Female)	0.0035	0.2219	1.0035	0.6495	1.5503	0.9875	ns
Ethnicity Asian (Reference: White)	1.3859	0.7198	3.9985	0.9754	16.3914	0.0542	ns
Ethnicity Black (Reference: White)	1.0909	0.7179	2.9770	0.7290	12.1568	0.1286	ns
Ethnicity Hispanic (Reference: White)	-0.0034	0.5126	0.9966	0.3649	2.7218	0.9947	ns
Ethnicity Other (Reference: White)	0.3836	1.0073	1.4676	0.2038	10.5681	0.7033	ns
Ethnicity Unknown (Reference: White)	-0.5681	1.0074	0.5666	0.0787	4.0809	0.5728	ns
Immunotherapy Agent Avelumab (Reference: Pembrolizumab)	1.3272	1.0571	3.7705	0.4749	29.9382	0.2093	ns
Immunotherapy Agent Ipilimumab (Reference: Pembrolizumab)	2.1307	1.0646	8.4207	1.0452	67.8428	0.0453	*
Immunotherapy Agent Ipilimumab/Nivolumab (Reference: Pembrolizumab)	0.3758	0.3660	1.4562	0.7107	2.9837	0.3045	ns
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.3352	0.3775	1.3982	0.6672	2.9302	0.3746	ns
Immunotherapy Agent Pembrolizumab/Ipilimumab (Reference: Pembrolizumab)	0.3696	0.6676	1.4471	0.3911	5.3549	0.5798	ns
Concurrent Chemotherapy	0.6541	0.7161	1.9233	0.4726	7.8265	0.3610	ns
Heart Disease	0.3702	0.2115	1.4480	0.9567	2.1916	0.0800	ns
Respiratory Condition	0.9011	0.3224	2.4623	1.3089	4.6320	0.0052	**
Diabetes	-0.0894	0.2327	0.9144	0.5795	1.4429	0.7007	ns
CKD	0.4744	0.2636	1.6070	0.9585	2.6943	0.0720	ns
Liver Failure	1.2652	0.5147	3.5439	1.2923	9.7182	0.0140	*
Immune Deficiency	-0.0346	0.2695	0.9660	0.5697	1.6382	0.8979	ns
English as Primary Language (Reference: No)	-0.4339	0.5117	0.6480	0.2377	1.7666	0.3965	ns
Previous history of malignancy at ICI Start	-0.2557	0.3000	0.7743	0.4301	1.3941	0.3940	ns
CNS Disease	0.2598	1.0068	1.2967	0.1802	9.3294	0.7964	ns
Treatment Year	-0.4273	0.1234	0.6523	0.5121	0.8308	0.0005	***

Supplementary Table 8: Cox univariable proportional hazards regression analysis of factors influencing overall survival in Stage IV melanoma patients receiving their first round of immunotherapy. The majority of variables have the same definitions as reported in **Supplementary Table 2.** "NRAS" - "GNAQ" are binary descriptions of whether patients had known mutations in these genes at the time of tumor biopsy. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001 unless otherwise noted. **(Fig 1d).**

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (relative to No mRNA Vaccination ever)	-1.0076	0.3575	0.3651	0.1812	0.7357	0.0048	**
Liver Metastasis at ICI Start	0.7319	0.2569	2.0790	1.2565	3.4397	0.0044	**
Steroid use within 1 month of ICI Initiation	0.6959	0.2923	2.0056	1.1310	3.5566	0.0173	*
Age at ICI Initiation	0.0371	0.0101	1.0378	1.0175	1.0586	0.0002	***
BRAF	-0.5383	0.2559	0.5837	0.3535	0.9640	0.0354	*
GNAQ	1.2506	0.7694	3.4925	0.7730	15.7790	0.1041	ns
ECOG	0.4365	0.1763	1.5472	1.0951	2.1860	0.0133	*
Immunotherapy Agent Avelumab (Reference: Pembrolizumab)	0.1541	1.1034	1.1666	0.1342	10.1430	0.8889	ns
Immunotherapy Agent Ipilimumab (Reference: Pembrolizumab)	-0.1323	1.2936	0.8761	0.0694	11.0564	0.9185	ns
Immunotherapy Agent Ipilimumab/Nivolumab (Reference: Pembrolizumab)	-0.0951	0.3996	0.9093	0.4155	1.9902	0.8120	ns
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.1160	0.3882	1.1230	0.5247	2.4033	0.7651	ns
Immunotherapy Agent Pembrolizumab/Ipilimumab (Reference: Pembrolizumab)	0.4389	0.7013	1.5511	0.3923	6.1322	0.5314	ns
Respiratory Condition	0.7733	0.3537	2.1669	1.0833	4.3343	0.0288	*
Liver Failure	1.2745	0.5375	3.5771	1.2473	10.2585	0.0177	*
Treatment Year	-0.2069	0.1382	0.8131	0.6202	1.0660	0.1343	ns

Supplementary Table 9: Cox multivariable proportional hazards regression analysis of factors influencing overall survival in Stage IV melanoma patients receiving first-line immunotherapy. This multivariable analysis includes the factors in the univariable analysis that had a significant relationship with overall survival alone in the patient population. See **Supplementary Table 8** for descriptions of variables included in analysis. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001 unless otherwise noted. **(Fig 1d).**

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (relative to No mRNA Vaccination ever)	-0.4437	0.2171	0.6416	0.4193	0.9820	0.0410	*
Brain Metastasis at ICI Start	0.2023	0.1920	1.2242	0.8403	1.7834	0.2920	ns
Liver Metastasis at ICI Start	0.4056	0.1940	1.5001	1.0256	2.1942	0.0366	*
Steroid use within 1 month of Vaccination	-0.4324	0.4984	0.6489	0.2443	1.7236	0.3856	ns
Steroid use within 1 month of ICI Initiation	0.3890	0.2048	1.4755	0.9878	2.2042	0.0575	ns
Age at ICI Initiation	0.0080	0.0063	1.0081	0.9958	1.0205	0.2002	ns
NRAS	-0.0768	0.2021	0.9261	0.6232	1.3762	0.7039	ns
BRAF	-0.1157	0.1704	0.8908	0.6378	1.2440	0.4973	ns
KIT	0.3894	0.2654	1.4761	0.8773	2.4835	0.1424	ns
PTEN	0.2188	0.2907	1.2445	0.7040	2.2003	0.4518	ns
GNA11	1.2315	0.5133	3.4263	1.2528	9.3709	0.0164	*
GNAQ	0.9556	0.5849	2.6002	0.8263	8.1821	0.1023	ns
ECOG	0.4114	0.1273	1.5089	1.1756	1.9367	0.0012	**
Gender Male (Reference: Female)	-0.1850	0.1724	0.8311	0.5928	1.1652	0.2832	ns
Ethnicity Asian (Reference: White)	2.2764	0.7350	9.7414	2.3067	41.1380	0.0020	**
Ethnicity Black (Reference: White)	0.9127	0.5869	2.4911	0.7885	7.8697	0.1199	ns
Ethnicity Hispanic (Reference: White)	0.5003	0.3651	1.6491	0.8063	3.3730	0.1706	ns
Ethnicity Other (Reference: White)	1.4663	1.0121	4.3333	0.5961	31.4992	0.1474	ns
Ethnicity Unknown (Reference: White)	-1.6658	1.0039	0.1890	0.0264	1.3524	0.0971	ns
Immunotherapy Agent Avelumab (Reference: Pembrolizumab)	1.2632	1.0325	3.5368	0.4674	26.7606	0.2212	ns
Immunotherapy Agent Ipilimumab (Reference: Pembrolizumab)	2.3566	1.0461	10.5545	1.3584	82.0057	0.0243	*
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.1451	0.2740	1.1561	0.6757	1.9780	0.5965	ns
Immunotherapy Agent Ipilimumab/Nivolumab (Reference: Pembrolizumab)	0.2351	0.2650	1.2651	0.7525	2.1266	0.3750	ns
Immunotherapy Agent Pembrolizumab/Ipilimumab (Reference: Pembrolizumab)	0.3417	0.5065	1.4074	0.5215	3.7981	0.4999	ns
Concurrent Chemotherapy	0.3639	0.5849	1.4389	0.4573	4.5277	0.5339	ns
Heart Disease	0.3331	0.1647	1.3953	1.0104	1.9269	0.0431	*
Respiratory Condition	0.6279	0.3021	1.8737	1.0365	3.3871	0.0377	*
Diabetes	0.1943	0.1768	1.2144	0.8588	1.7172	0.2717	ns
CKD	0.4658	0.2138	1.5933	1.0479	2.4224	0.0293	*
Liver Failure	1.2231	0.4599	3.3979	1.3796	8.3688	0.0078	**
Immune Deficiency	0.4713	0.1984	1.6021	1.0860	2.3634	0.0175	*
English as Primary Language (Reference: No)	-0.2536	0.4553	0.7760	0.3179	1.8941	0.5776	ns
Previous history of malignancy at ICI Start	-0.4072	0.2409	0.6655	0.4151	1.0670	0.0909	ns
CNS Disease	-0.4242	1.0039	0.6543	0.0915	4.6804	0.6726	ns
Treatment Year	-0.1285	0.0848	0.8794	0.7447	1.0385	0.1297	ns

Supplementary Table 10: **Cox univariable proportional hazards regression analysis of factors influencing progression-free survival in Stage IV melanoma patients receiving their first round of immunotherapy.** See **Supplementary Table 8** for descriptions of variables included in analysis. Univariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. *p<0.05, **p<0.01, ***p<0.001 unless otherwise noted. **(Fig 1e).**

Variable	Beta	St. Error	HR	2.5% CI	97.5 % CI	p value	P value interpretation
COVID mRNA vaccination within 100 days of ICI (relative to No mRNA Vaccination ever)	-0.4690	0.2264	0.6256	0.4014	0.9751	0.0383	*
Liver Mets at ICI Start	0.2265	0.2302	1.2541	0.7987	1.9693	0.3253	ns
GNA11	0.8993	0.5974	2.4579	0.7621	7.9270	0.1323	ns
ECOG	0.3353	0.1425	1.3983	1.0575	1.8489	0.0187	*
Ethnicity Asian (Reference: White)	2.2848	0.8096	9.8240	2.0097	48.0231	0.0048	**
Ethnicity Black (Reference: White)	1.0057	0.6164	2.7339	0.8167	9.1515	0.1028	ns
Ethnicity Hispanic (Reference: White)	0.6866	0.3772	1.9869	0.9486	4.1616	0.0687	ns
Ethnicity Other (Reference: White)	1.3578	1.0296	3.8877	0.5167	29.2493	0.1872	ns
Ethnicity Unknown (Reference: White)	-1.5399	1.0133	0.2144	0.0294	1.5624	0.1286	ns
Immunotherapy Agent Avelumab (Reference: Pembrolizumab)	0.4880	1.0992	1.6290	0.1889	14.0472	0.6571	ns
Immunotherapy Agent Ipilimumab (Reference: Pembrolizumab)	2.6419	1.0790	14.0400	1.6942	116.3530	0.0143	*
Immunotherapy Agent Nivolumab (Reference: Pembrolizumab)	0.1736	0.2866	1.1896	0.6783	2.0862	0.5447	ns
Immunotherapy Agent Ipilimumab/Nivolumab (Reference: Pembrolizumab)	0.0608	0.2929	1.0627	0.5986	1.8867	0.8355	ns
Immunotherapy Agent Pembrolizumab/Ipilimumab (Reference: Pembrolizumab)	0.5242	0.5282	1.6891	0.5999	4.7557	0.3210	ns
Heart Disease	0.1894	0.1811	1.2086	0.8475	1.7234	0.2955	ns
Respiratory Condition	0.1532	0.3593	1.1656	0.5764	2.3571	0.6698	ns
Chronic Kidney Disease	0.2572	0.2446	1.2933	0.8008	2.0887	0.2930	ns
Liver Failure	1.2530	0.4733	3.5007	1.3846	8.8509	0.0081	**
Immune Deficiency	0.3799	0.2328	1.4621	0.9265	2.3075	0.1027	ns

Supplementary Table 11: Cox multivariable proportional hazards regression analysis of factors influencing progression-free survival in Stage IV melanoma patients receiving their first round of immunotherapy. This multivariable analysis included the factors in the univariable analysis that had a significant relationship with progression-free survival alone in the patient population. See **Supplementary Table 8** for descriptions of variables included in analysis. *$p<0.05$, **$p<0.01$, ***$p<0.001$ unless otherwise noted. Multivariable Cox proportional hazards regression (two-sided) was used to estimate hazard ratios and P values. **(Fig 1e).**

Marker	Color	Clone	Company	Cat#	uI/100 µL
CD45	BUV395	30-F11	Thermo	363-0451-82	0.5
CD11c	BUV496	N418	BD	750450	0.125
CD11c	RY703	N418	BD	570292	0.125
CD80	BUV737	16-10A1	BD	612773	1
MHC-II	PAC BLUE	M5/114.15.2	BioLegend	107620	0.125
Ly6G	BV605	1A8	BioLegend	127629	0.625
CD163	BV711	S15049I	BioLegend	155325	0.5
Ly6C	BV785	HK1.4	BioLegend	128041	1.25
CD206	AF488	C068C2	BioLegend	141710	0.8
CD86	RB613	B7-2	BD	759079	1
F4/80	RB780	T45-2342	BD	569223	0.25
CD11B	RY703	M1/70	BD	571473	0.1
CD11B	RB705	M1/70	BD	755202	0.1
PD-L1	APC	485	Thermo Fisher	MA5-46763	4
H2Kb Siinfekl	PE	25-D1.16	Biolegend	141604	1.25
L/D	NIR	N/A	Thermo Fisher	L10119	0.5

Supplementary Table 12: Antibodies utilized in myeloid panels for murine experiments. (Fig 2f-o, Extended Data Fig. 9a-b).

Marker	Color	Clone	Company	Cat#	uL/100 µL
CD3	BUV395	17A2	BD	740268	1
CD161	BUV563	PK136	BD	741233	1
CD127	BUV737	SB/199	BD	612841	0.6
CD4	PAC BLUE	GK1.5	BioLegend	100428	0.3
PD-1	BV605	J43	BD	563059	0.3
CD25	BV785	PC61	BioLegend	102051	0.5
CD44	AF488	IM7	BioLegend	103016	0.3
KLRG1	RB613	2F1	BD	758385	1.25
CD69	RB705	H1.2F3	BD	756896	1.25
CD62L	RB780	MEL-14	BD	569209	0.3
LAG-3	PE	C9B7W	BD	552380	0.6
TIM-3	APC	B8.2C12	BioLegend	134008	0.6
CD8A	AF700	53-6.7	BD	557959	0.3
L/D	NIR	N/A	Thermo Fisher	L10119	0.5

Supplementary Table 13: **Antibody panel for murine T cell markers. (Fig. 3a-b, Extended Data Fig. 9d).**

Marker	Color	Clone	Company	Cat#	ul/100 µL
CD40L	FITC	SA047C3	BD	157006	1
CD25	PE-CF594	PC61	BioLegend	101920	2.5
CD69	APC	H1.2F3	Biolegend	104514	3.3
CD3	AF700	17A2	Biolegend	100216	1
CD8A	APC-H7	53-6.7	BD	560182	2
CD4	Pac Blue	RM4-4	BioLegend	116008	1
4-1BB	PE	17B5	BioLegend	106106	1.25

Supplementary Table 14: Antibody panel for AIM assay. (Fig 3d).

Marker	Clone	Company	Cat#	Dilution
CD274 (PD-L1)	2B11D11	Proteintech	66248-1-Ig	1:100
SOX10	SP267	Abcam	ab227680	1:200
CD3	145 2C11	BD	553057	1:100
CD8	pAb	Invitrogen	PA5-81344	1:1000
PD-1	J121	eBioscience	14-2798-82	1:100
Goat anti-mouse AF488	pAB	Invitrogen	A11001	1:1000
Goat anti-rabbit AF564	pAB	Invitrogen	A11012	1:1000
Goat anti-hamster AF647	pAB	Invitrogen	A78967	1:1000

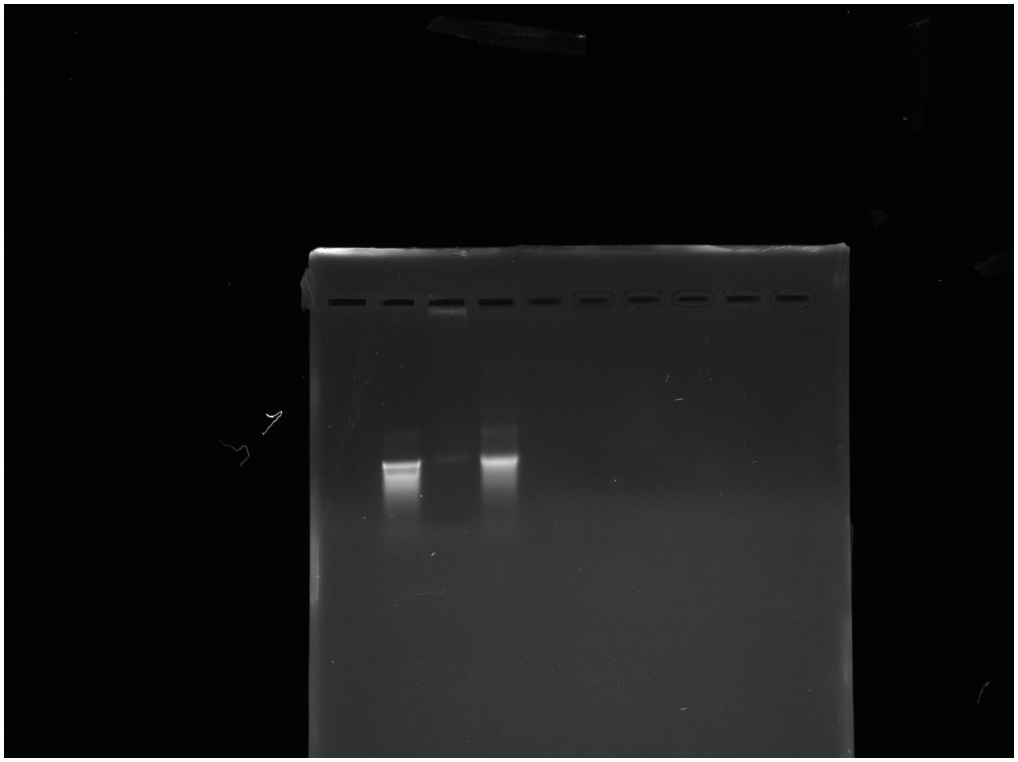
Supplementary Table 15: **Antibody panel for immunofluorescence. (Fig 3e-f)**

Marker	Color	Clone	Company	Cat#	Volume (uL/100uL)
CD14	APC/Fire™ 810	63D3	BioLegend	367156	0.15
CD19	PE/Fire™ 640	HIB19	BioLegend	302274	1.25
CD56	BV711	NCAM16.2	BD Biosciences	563169	0.63
PD-L1	RB705	MIH1	BD Biosciences	757550	0.8
CD16	BUV496	3G8	BD Biosciences	612944	0.63
CD11c	BUV563	B-ly6	BD Biosciences	741358	0.3
CD11b	BUV661	M1/70	BD Biosciences	612977	1.25
HLA-DR	BV510	G46-6	BD Biosciences	563083	2.5
CD80	BV786	L307.4	BD Biosciences	564159	3
CD86 (B7-2)	RB780	2331 (FUN-1)	BD Biosciences	755689	1.25
CD45	R718	HI30	BD Biosciences	566961	0.625
CD3	APC-H7	SK7	BD Biosciences	560176	0.625
CD56	BV711	NCAM16.2	BD Biosciences	563169	0.63

Supplementary Table 16: Antibody panel for human myeloid cells. (Fig. 4e-f).

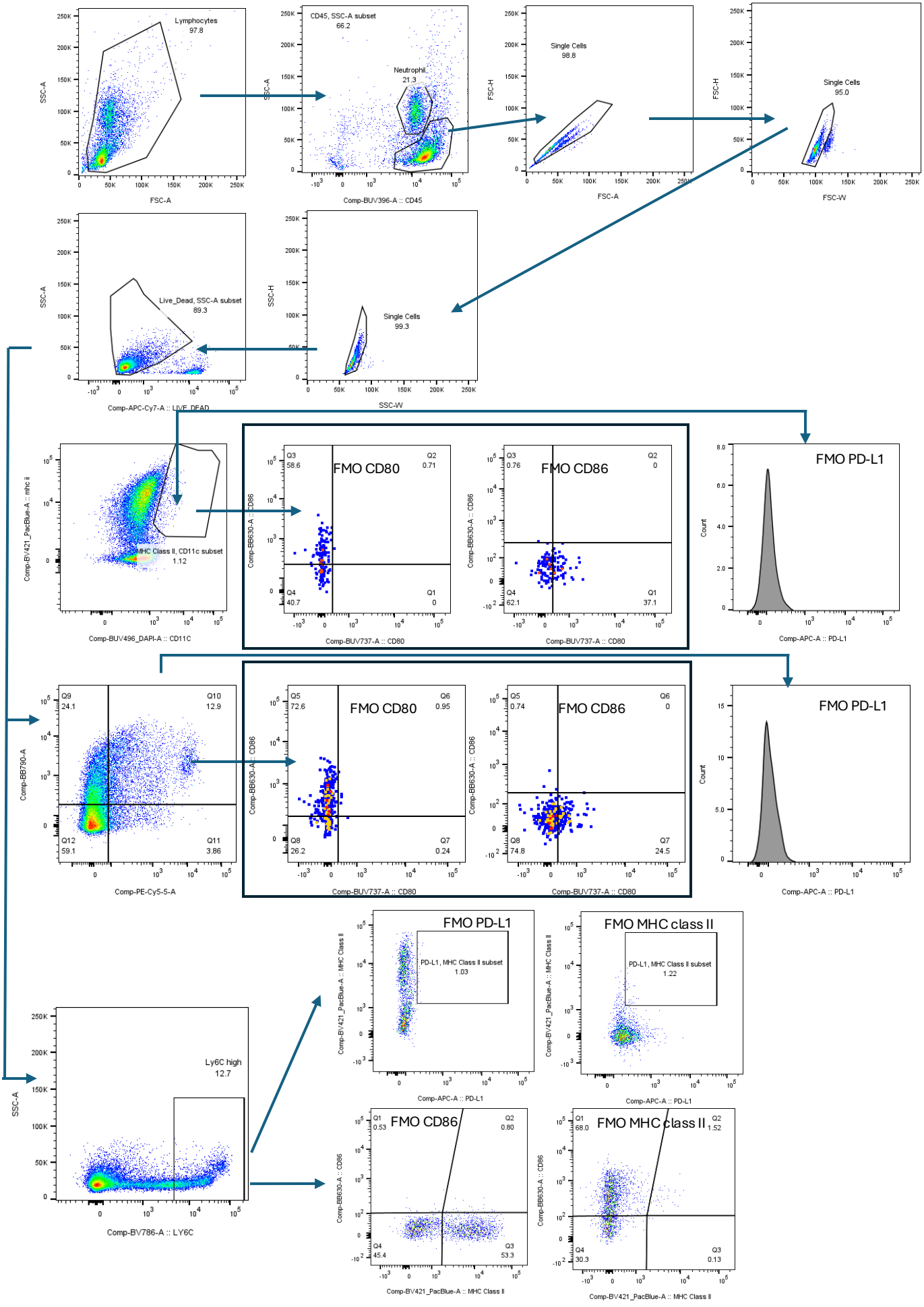
Marker	Color	Clone	Company	Cat#	Volume (uL/100uL)
CD14	APC/Fire™ 810	63D3	BioLegend	367156	0.15
PD-1	Brilliant Violet 421™	EH12.2H7	BioLegend	329920	3
Human TruStain FcX™			BioLegend	422302	5
CD25	PE/Cyanine 7	BC96	BioLegend	302612	5
CD19	PE/Fire™ 640	HIB19	BioLegend	302274	1.25
CD8	PE/Fire™ 700	SK1	BioLegend	344766	1.25
PD-L1	PerCP/Cyanine5.5	29E.2A3	BioLegend	329738	5
CD16	BUV496	3G8	BD Biosciences	612944	0.63
CD11c	BUV563	B-ly6	BD Biosciences	741358	0.3
CD11b	BUV661	M1/70	BD Biosciences	612977	1.25
CCR7 (CD197)	BUV737	3D12	BD Biosciences	741786	0.625
CD15	BUV805	7C3.RMAB	BD Biosciences	568935	2.5
CD4	BV480	L200	BD Biosciences	566148	0.16
HLA-DR	BV510	G46-6	BD Biosciences	563083	2.5
GITR (CD357)	BV605	V27-580	BD Biosciences	747664	3
CD127	BV650	hIL-7R-M21	BD Biosciences	563225	2.5
CD56	BV711	NCAM16.2	BD Biosciences	563169	0.63
CD80	BV786	L307.4	BD Biosciences	564159	3
Granzyme A	FITC	CB9	BD Biosciences	568661	5
Granzyme B	RB613	GB11	BD Biosciences	571117	0.625
CD86 (B7-2)	RB780	2331 (FUN-1)	BD Biosciences	755689	1.25
CD178	PE	NOK-1	BD Biosciences	564261	3
CD33	RY610	HIM3-4	BD Biosciences	758223	2.5
CD68	Alexa 647	Y1/82A	BD Biosciences	562111	3
CD45	R718	HI30	BD Biosciences	566961	0.625
CD3	APC-H7	SK7	BD Biosciences	560176	0.625
Brilliant Stain Buffer Plus			BD Biosciences	566385	10
CD45RA	BUV395	HI100	BD Biosciences	568712	0.3
CD69	BUV615	FN50	BD Biosciences	751501	3

Supplementary Table 17:Antibody panel for human lymphocytes. (Fig. 4g-h).

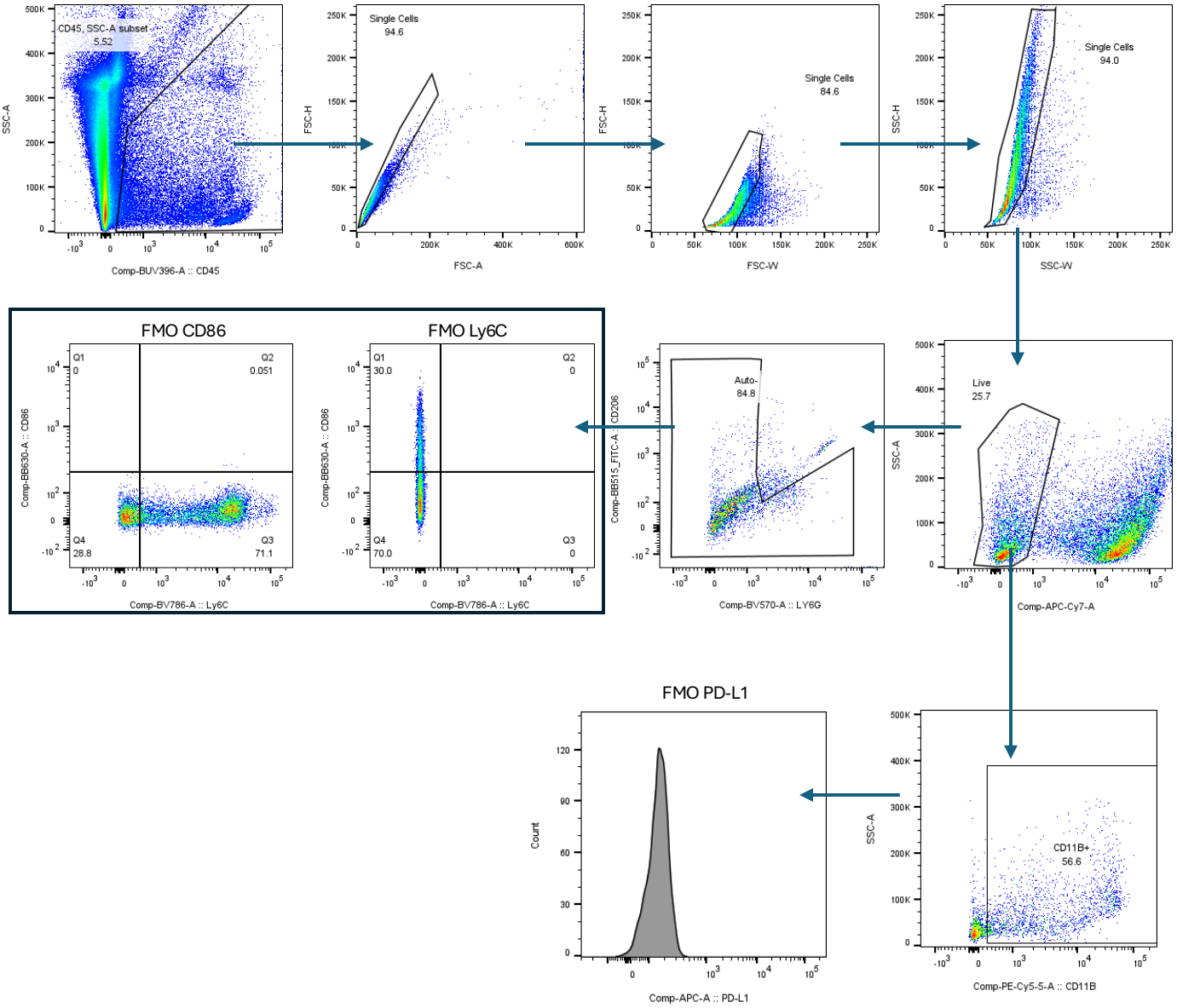


Supplementary Figure 1: **Original image of agarose gel electrophoresis. (EDF 4d).**

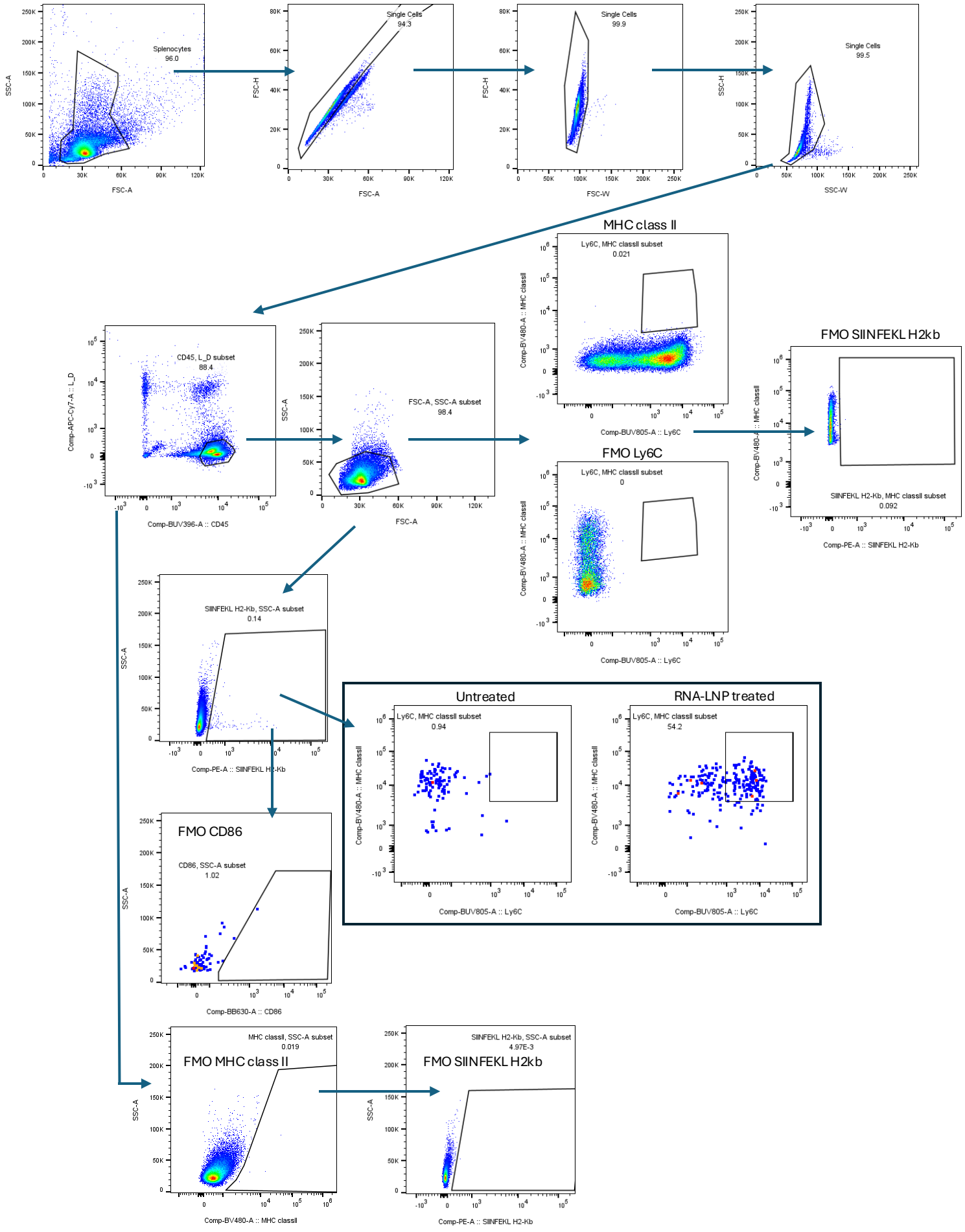
Gating strategy for splenic myeloid panel



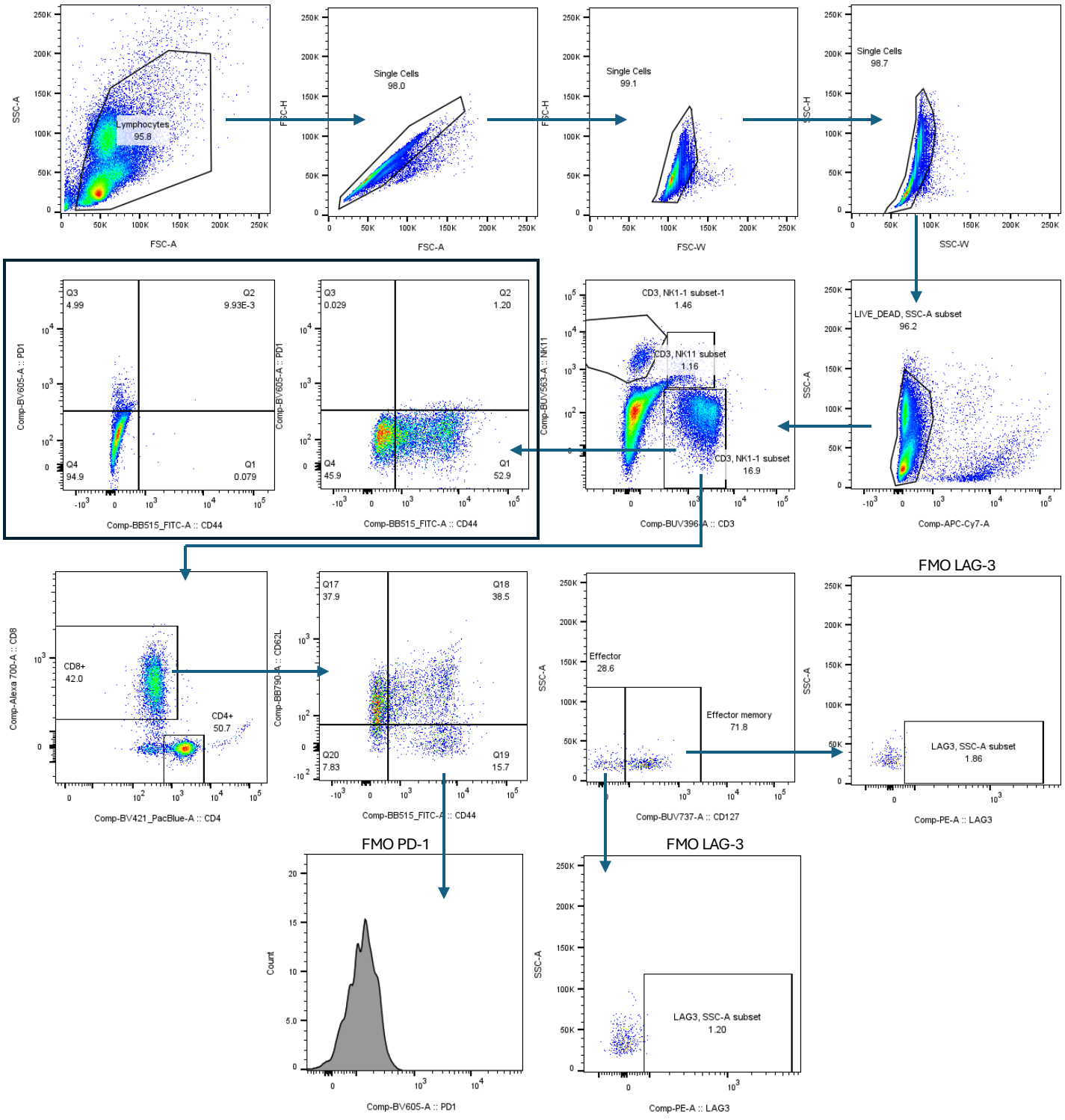
Supplementary Figure 2: **Gating strategy for murine splenic myeloid panel (Fig 2f-i, EDF9 a-b).**



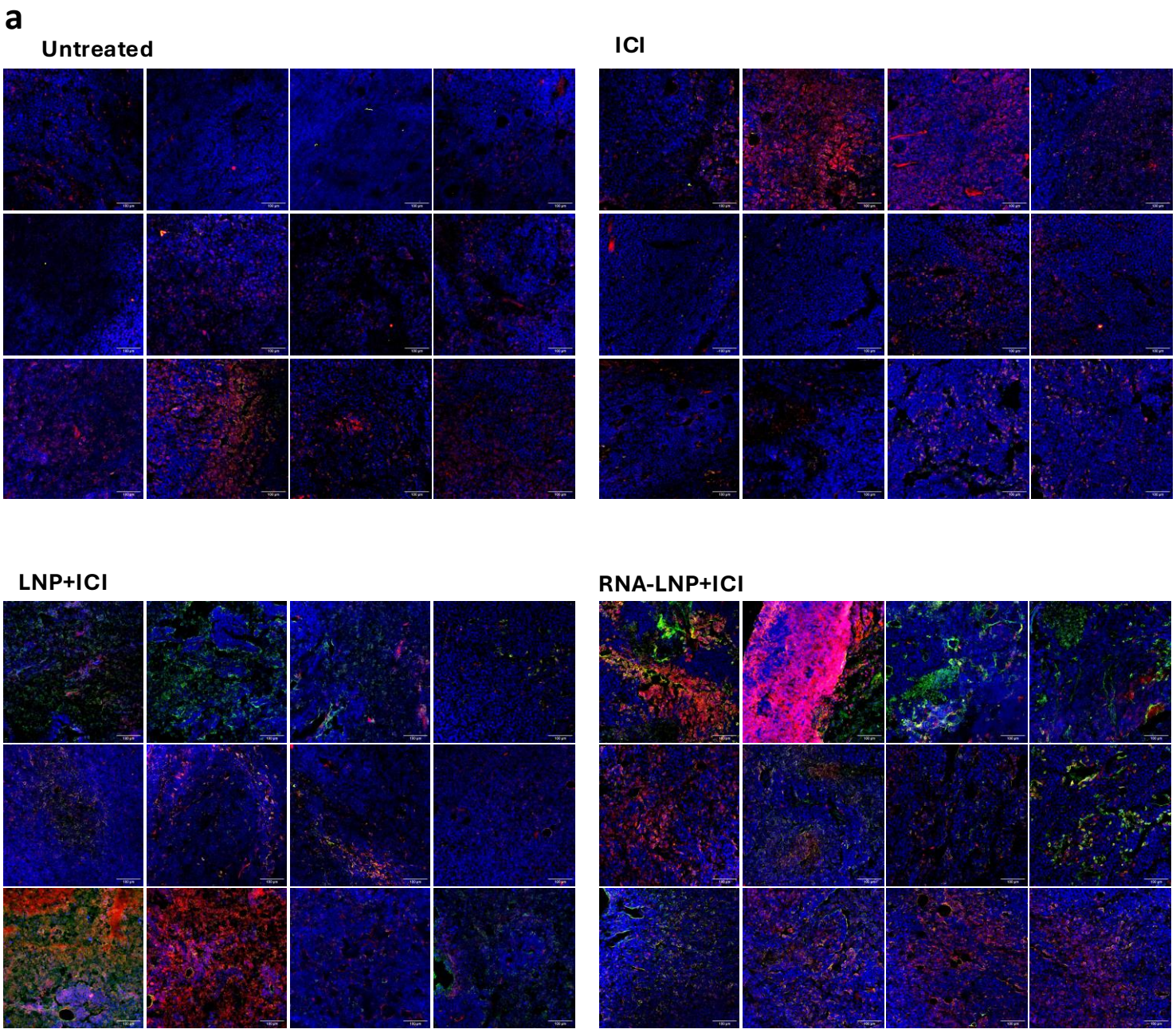
Supplementary Figure 3: **Gating strategy for murine tumor myeloid panel (EDF9 c)**



Supplementary Figure 4: Gating strategy for SIINFEKL presentation (Fig 2j-o).

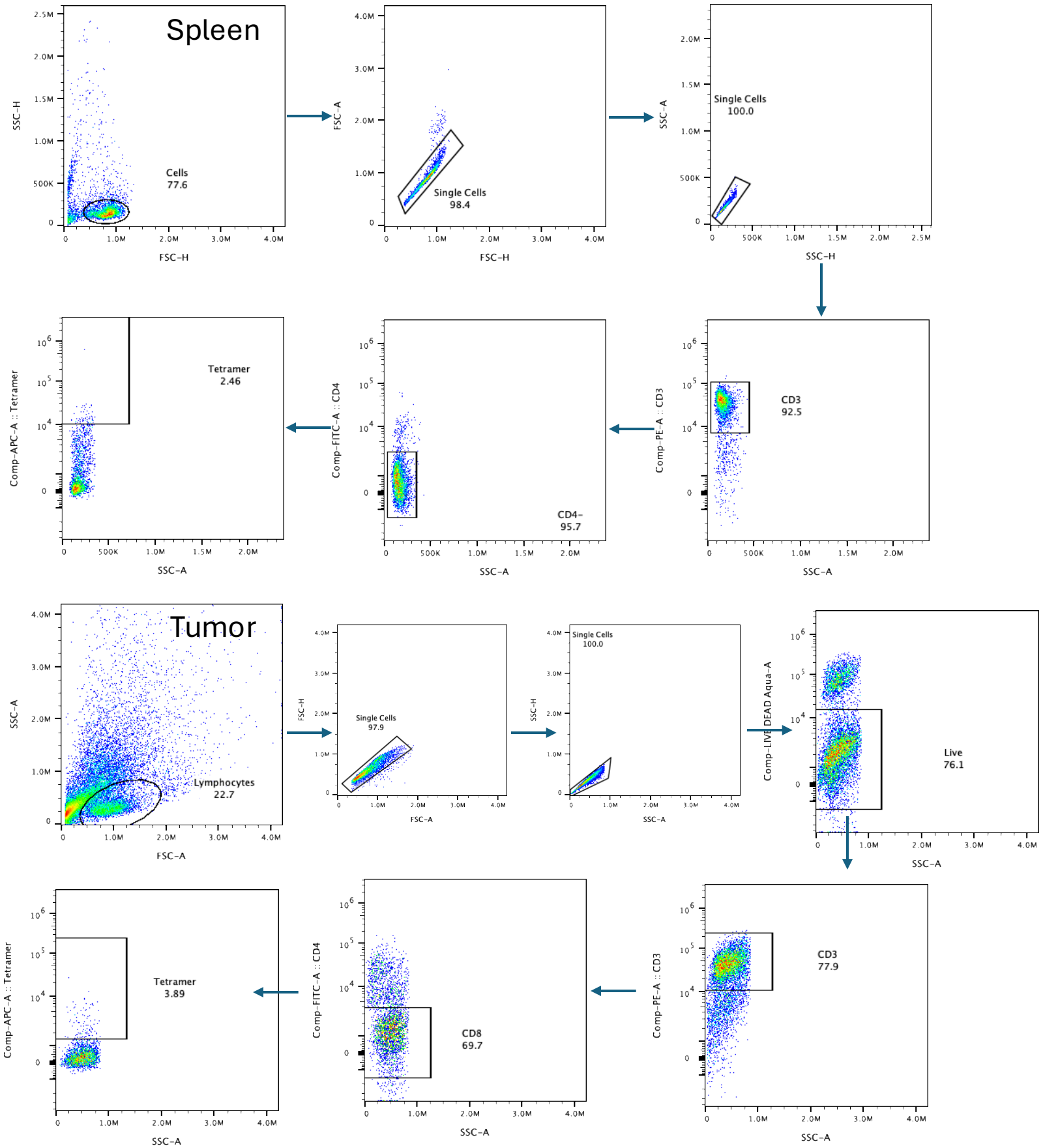


Supplementary Figure 5: Gating strategy for murine T cell panel (Fig 3a-b, g, EDF9 d-f)



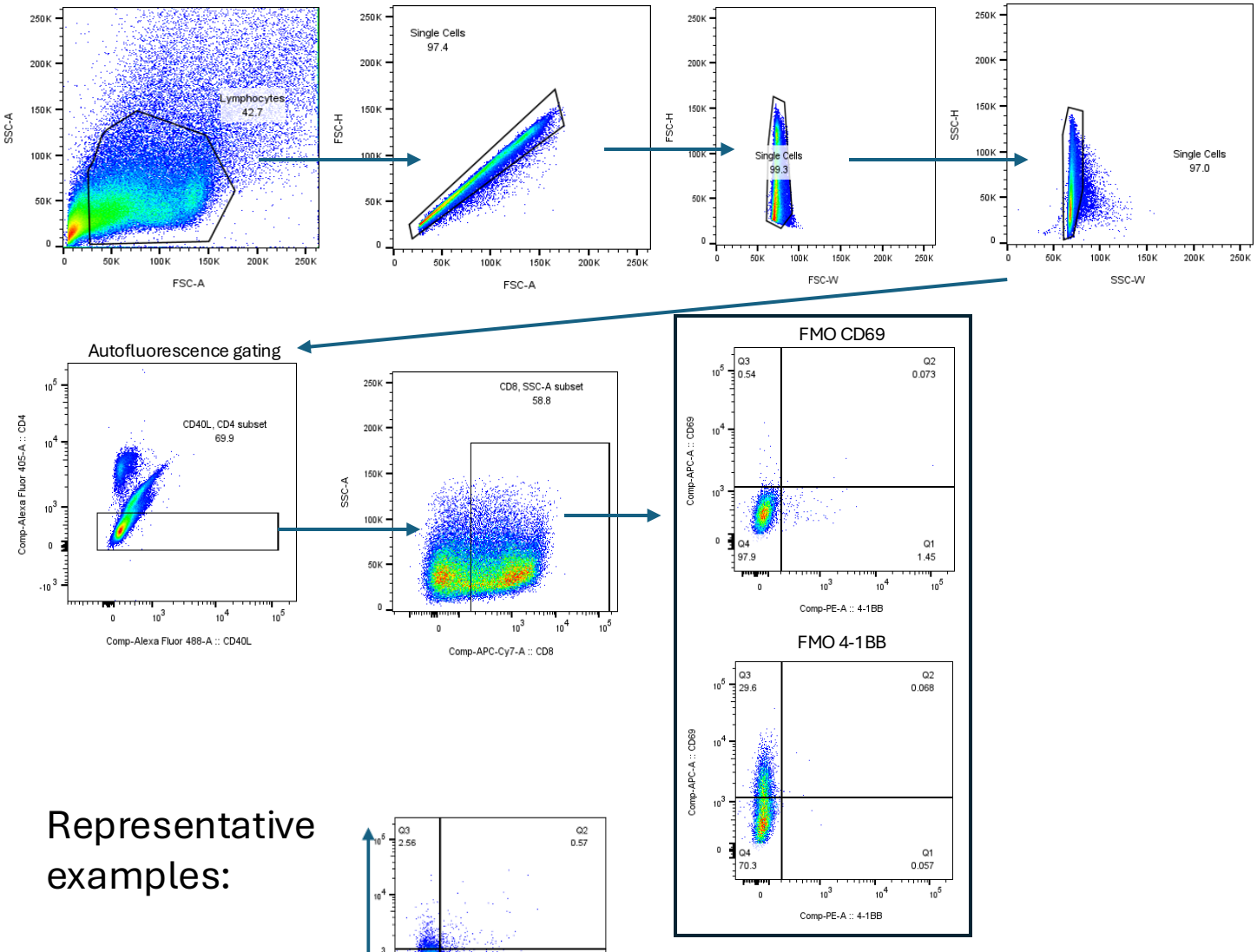
Supplementary Figure 6: Representative images of PD-1 expression in each treatment group. **a**, Confocal images of representative slices used to quantify PD-1 expression (Green) on CD8+ (Red) tumor cells in each group. Nuclei stained with DAPI appear blue. Each row of images represents 4 different frames collected from a single tumor. Images were collected by a blinded manner and frames were selected at random. **(EDF 9e-f).**

Gating strategy for tetramer assay

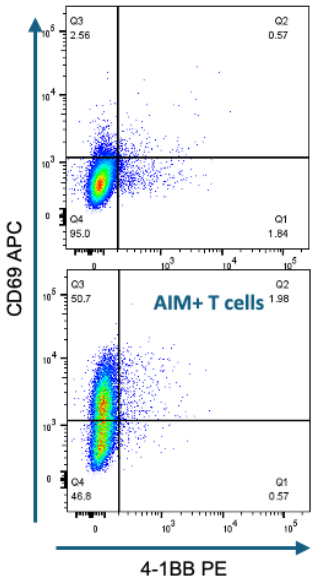


Supplementary Figure 7: Gating strategy for Tetramer Assay (Fig 3c, h)

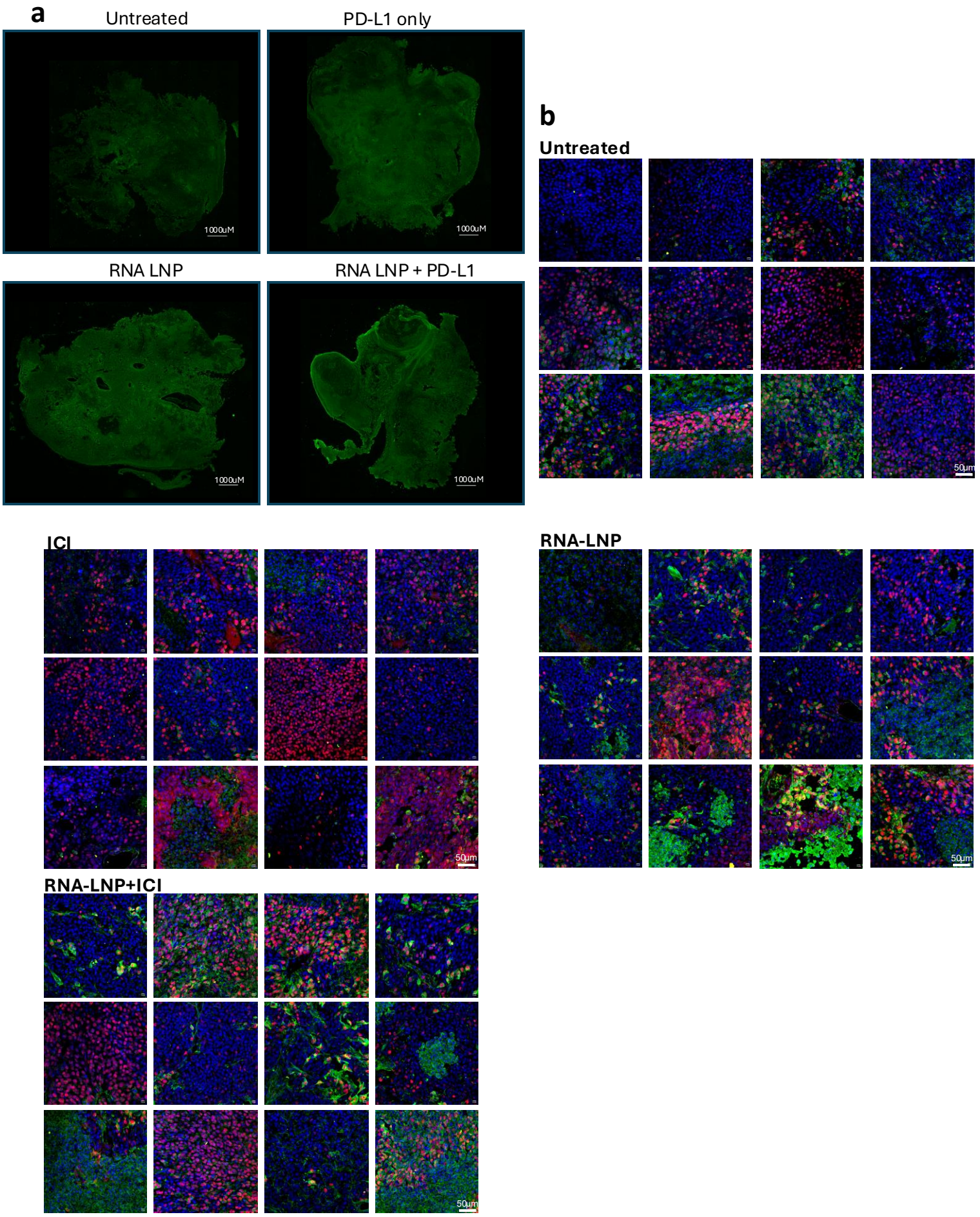
Gating strategy for AIM assay



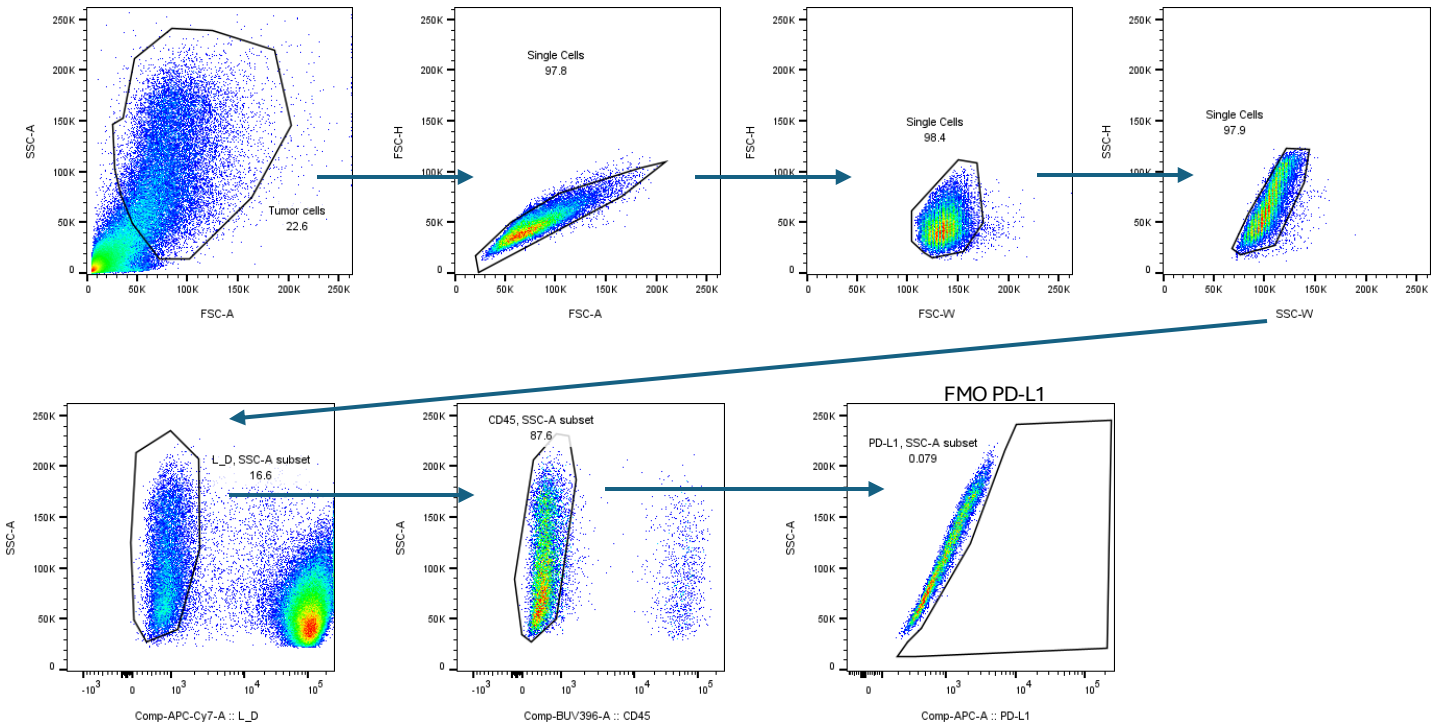
Representative examples:



Supplementary Figure 8: Gating strategy for AIM Assay (Fig 3d)

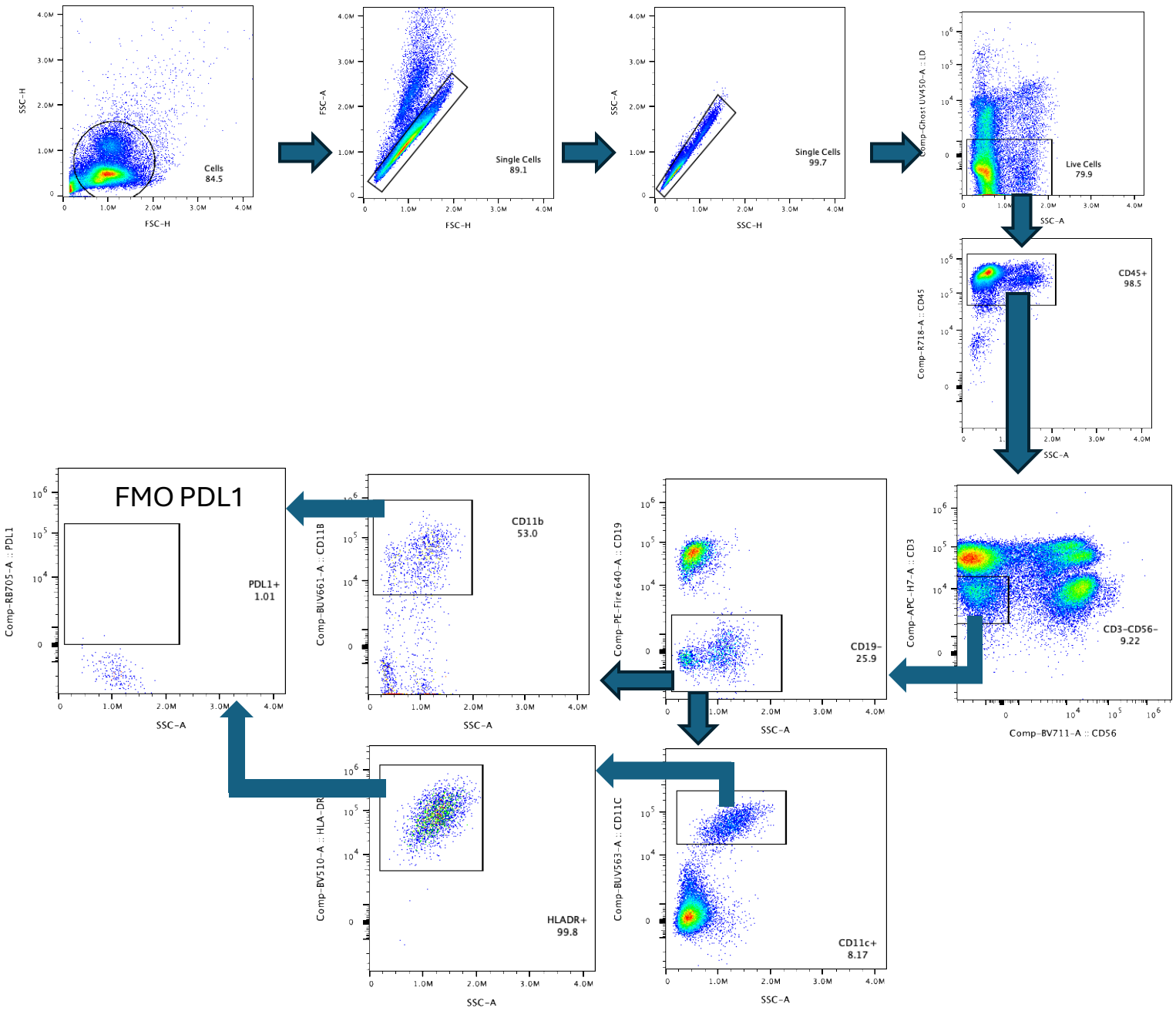


Supplementary Figure 9: Representative images of PD-L1 expression in each treatment group. **a**, Keyence imaging of PD-L1 expression from whole tumor slides harvested from animals after vaccine 3. **b**, Confocal images of representative slices used to quantify PDL1 expression (Green) on SOX10+ (Red) tumor cells in each group. Nuclei stained with DAPI appear blue. **(Fig. 3i-k; Extended Data Fig. 9g-h).**

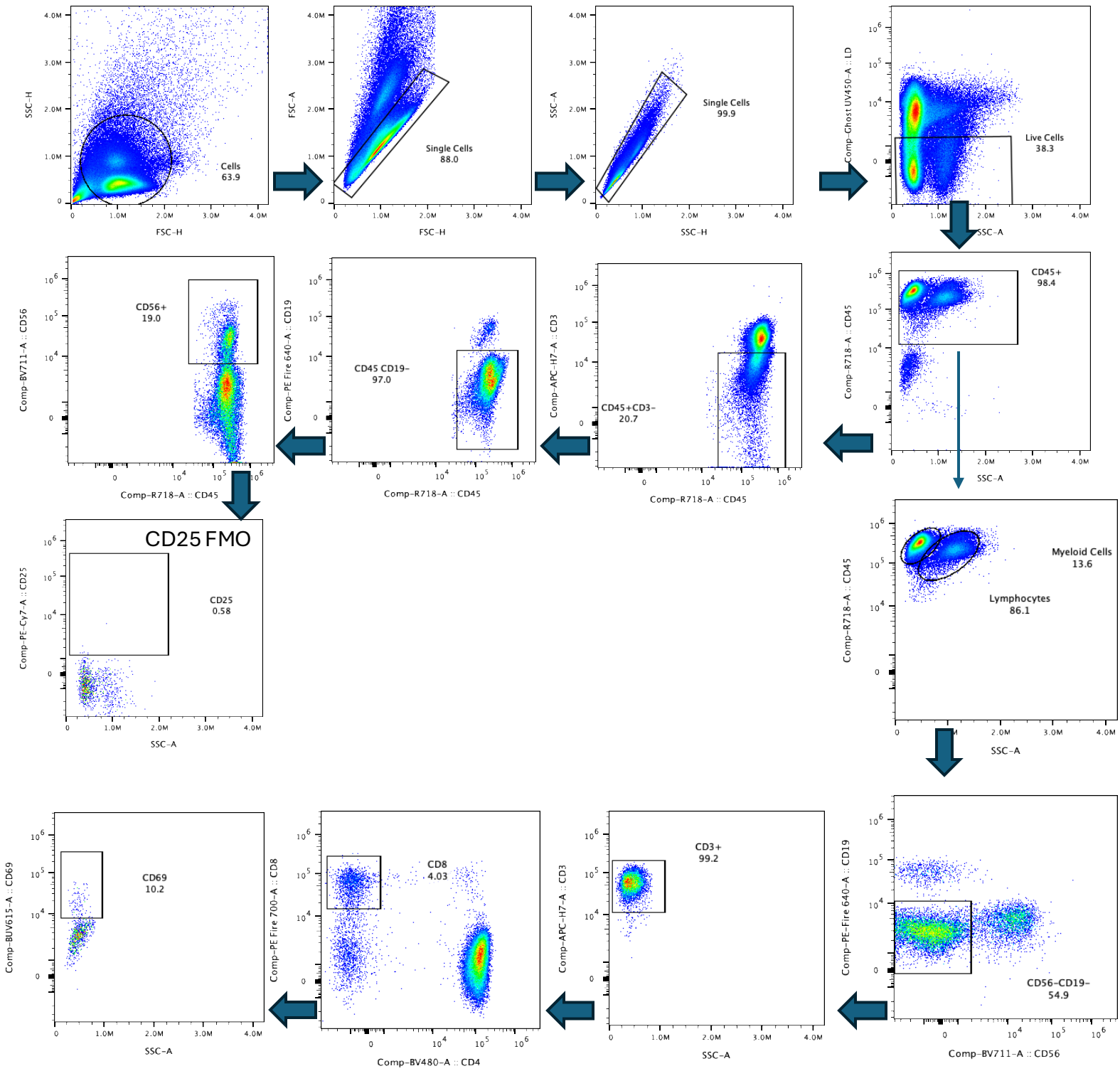


Supplementary Figure 10: Gating strategy for PD-L1 expression on murine tumors (Fig 3i, EDF9 h).

Supplemental Figure 11: Cytokine production in healthy subjects after Pfizer or Moderna SARS-COV-2 mRNA immunization at 24h. Volcano plots displaying the cytokines from the NULISA-Seq Inflammation Panel that are significantly different at 24 hours compared to baseline after controlling for multiple comparisons. Significant variables were defined as those with p<.05 and log2-Fold-Change with absolute value greater than 0.5 following linear modeling with fixed effect. Adjusted p values were calculated using moderated t-tests with FDR correction for multiple testing. **(Fig. 4 b-d, EDF 10b-d).**



Supplementary Figure 12: Gating strategy for human myeloid cells (Fig 4e,f, and EDF 10e,f)



Supplementary Figure 13: Gating strategy for human lymphocytes (Fig 4g,h and EDF 10g,h).