Supplementary Table 1

ID ICB	Age	Sex	Tumour Type	Treatment	Line of Therapy	UICC Stage	Number of Metastatic Sites	GRIm-Score*	Initial Treatment Response	Best Overall Response	PFS (months)
001	59	M	CUP	Nivolumab	3rd	IV	NA	2	PD	PD	3
002	60	M	HNSCC	Nivolumab	2nd	IVC	1	1	SD	SD	7
004	37	M	RCC	Nivolumab	2nd	IV	2	0	PR	PR	21
005	82	M	RCC	Nivolumab	2nd	IV	4	1	PR	PR	(4)
006	62	F	RCC	Nivolumab	3rd	IV	5	1	PD	PD	3
007	64	M	NSCLC	Pembrolizumab	1st	IVA	2	1	PR	PR	(7)
008	72	M	Melanoma	Ipilimumab/ Nivolumab	2nd	IV	1	1	SD	SD	13
010	35	F	RCC	Nivolumab	4th	IV	3	1	PD	PD	3
011	65	M	RCC	Ipilimumab/ Nivolumab	1st	IV	3	3	PD	PD	8
012	59	M	HNSCC	Nivolumab	3rd	IVC	1	2	PR	PR	(18+)
013	70	M	Colon Carcinoma	Pembrolizumab	2nd	IV	1	1	PR	PR	(18+)
014	70	M	HNSCC	Nivolumab	3rd	IVC	1	2	PR	PR	(10)
016	50	F	NSCLC	Pembrolizumab/ Carboplatin/ Pemetrexed	1st	IVC	6	0	PR	CR	(18+)
018	47	M	RCC	Nivolumab	4th	IV	6	1	PD	PD	2
019	71	M	NSCLC	Pembrolizumab/ Carboplatin/ Paclitaxel	1st	IVC	3	3	PR	PR	6
021	65	M	NSCLC/ RCC (synchronous)	Ipilimumab/ Nivolumab	1st	IVC/ IV	4	2	PD	PD	3
022	63	M	HNSCC	Nivolumab	4th	IVC	3	2	PD	PD	3
024	63	M	RCC	Nivolumab	2nd	IV	1	1	PR	PR	10
027	59	M	HNSCC	Nivolumab	3rd	IVC	4	2	PD	PD	2
028	49	M	RCC	Nivolumab	2nd	IV	4	1	PD	PD	3
030	78	F	HNSCC	Nivolumab	3rd	IVC	2	1	PR	CR	(17+)
032	52	M	HNSCC	Nivolumab	3rd	IVC	3	1	PD	PD	3
033	73	M	HNSCC	Nivolumab	3rd	IVC	1	1	SD	SD	5
034	75	M	HNSCC	Nivolumab	2nd	IVC	1	0	PD	PD	3
035	54	M	HNSCC	Nivolumab	3rd	IVA	0	0	PD	PD	3
038	75	M	HNSCC	Pembrolizumab	3rd	IVC	1	0	PR	CR	(14+)
040	45	M	Urothelial Carcinoma	Pembrolizumab	2nd	IV	1	1	PD	PD	2
041	65	M	RCC	Nivolumab	3rd	IV	5	0	PD	PD	3
042	53	M	RCC	Nivolumab	2nd	IV	1	1	SD	CR	(15+)
044	58	M	RCC	Pembrolizumab/ Axitinib	1st	IV	2	0	PD	PD	4
045	55	F	HNSCC	Pembrolizumab	1st	IVC	1	0	PR	PR	12
046	73	M	HNSCC	Nivolumab	3rd	IVC	1	2	PD	PD	3
047	63	M	HNSCC	Pembrolizumab/ Cisplatin/ 5-Fluorouracil	1st	IVA	0	2	PD	PD	3
050	64	F	HNSCC	Pembrolizumab	1st			0	PD	PD	3
051	62	F	Melanoma	Ipilimumab/ Nivolumab	1st	IV	1	1	PR	PR	(14+)
056	76	F	RCC	Nivolumab	3rd	IV	5	1	PD	PD	2
057	79	M	HNSCC	Pembrolizumab	1st	(IVC)	1	0	PD	PD	3
060	68	M	HNSCC	Pembrolizumab	2nd	IVA	0	0	PR	PR	(5+)
061	55	M	CUP	Pembrolizumab	1st	IV	NA	-	PR	PR	(6+)
063	74	M	HNSCC	Pembrolizumab	1st	III	0	1	PR	PR	(3+)
064	54	M	RCC	Nivolumab	2nd	IV	4	1	PD	PD	3
065	72	F	HNSCC	Pembrolizumab	1st	IVC	4	1	PR	PR	5
066	65	F	HNSCC	Pembrolizumab	2nd	IVC	2	0	PD	PD	2

Tab. S1: Individual patient characteristics. Initial treatment response was evaluated according to iRECIST criteria and clinical assessment by week 16 upon ICB initiation. Time to disease progression is presented in brackets for patients who have not experienced progressive disease yet or have died despite positive radiologic response to therapy. CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease.

Supplementary Table 2: Immune cell population panel

Immunocyte subset	Gating strategy	Abbreviation
Leucocytes	$CD45^+$	Leuco
Lymphocytes	$CD45^+$, Lymphocytes (FSC/SSC)	Lympho
T cells	$CD45^+$, Lymphocytes (FSC/SSC), $CD3^+$	CD3
• **$CD8^+$ T cytotoxic cells**	• $CD8^+$, $CD4^-$	CD8
○ **$CD28^-$ $CD8^+$ T cells**	○ $CD27^-$, $CD28^-$	CD8_CD28neg
○ **Activation status**	○ $CD38^+$	CD8_CD38
• **$CD4^+$ T helper cells**	• $CD8^-$, $CD4^+$	CD4
○ **Regulatory T cells (Tregs)**	○ $CD25^+$, $CD127^-$	Tregs
· **Activation status**	· $CD38^+$	Tregs_CD38
○ **Conventional T helper cells**	○ $CD25^-$	CD4_conv
· **Activation status**	· $CD38^+$	CD4_CD38
• **γδ T cells**	• $CD8^{high-}$, $CD4^-$, $TCR\gamma\delta^+$	gdT
• **$CD4^+$ $CD8^+$ T cells**	• $CD8^+$, $CD4^+$	CD4CD8
B cells	$CD45^+$, Lymphocytes (FSC/SSC), $CD3^-$, $CD19^+$, $CD28^-$	B_cells
• **Naïve B cells**	• $CD27^-$, IgD^+	B_Naive
• **Transitional B cells**	• $CD27^+$, IgD^+	B_Trans
• **Memory B cells**	• $CD27^+$, IgD^-	B_Mem
• **Double-negative B cells**	• $CD27^-$, IgD^-	B_DN
• **Plasmablasts**	• $CD27^+$, $CD38^+$	
NK cells	$CD45^+$, Lymphocytes (FSC/SSC), $CD3^-$, $CD19^-$, $CD56^{+/++}$	NK
• **$CD56^{bright}$ NK cells**	• $CD56^{++}$	NK_br
• **$CD56^{dim}$ NK cells**	• $CD56^+$	NK_dim
• **Activation status**	• $CD38^+$	NK_CD38
Monocytes	$CD45^+$, non-Lymphocytes (FSC/SSC), $CD3^-$, $CD56^-$, $CD16^{dim}$, $CD14^+$	Mono
• **Classical monocytes**	• $CD16^-$	Mo_cl
• **Nonclassical monocytes**	• $CD16^+$	Mo_infl
Dendritic cells	$CD45^+$, Lymphocytes (FSC/SSC), $CD3^-$, $CD19^-$, CD56-, $CD14^-$, $HLA\text{-}DR^+$	
• **Plasmocytoid DC**	• $CD123^+$	pDC
• **Myeloid DC**	• $CD123^-$	mDC
Granulocytes	$CD45^+$, non-Lymphocytes (FSC/SSC), $CD14^-$	Granulo
Neutrophils	$CD45^+$, non-Lymphocytes (FSC/SSC), $CD14^-$, $CD16^+$	Neutro
Eosinophils	$CD45^+$, non-Lymphocytes (FSC/SSC), $CD14^-$, $CD16^-$, $HLA\text{-}DR^-$, $CD38^-$	Eosino
Basophils	$CD45^+$, Lymphocytes (FSC/SSC), $CD3^-$, $CD19^-$, $CD56^-$, $CD14^-$, $CD123^+$, $HLA\text{-}DR^-$	Baso

Supplementary Table 3: T cell population panel

T cell subset	Gating strategy	Abbreviation
CD3+ T cells	Lymphocytes (FSC/SSC), Singlets, $CD3^+$	CD3
• **$CD4^+$ T cells**	• $CD4^+$, $CD8^-$	CD4
○ **Naïve**	○ $CD45RA^+$, $CCR7^+$	CD4_Naive
· **Recent thymic emigrants**	· $CD31^+$	CD4_RTE
○ **Central memory**	○ $CD45RA^-$, $CCR7^+$	CD4_CM
○ **Effector memory**	○ $CD45RA^-$, $CCR7^-$	CD4_EM
○ **TEMRA**	○ $CD45RA^+$, $CCR7^-$	CD4_TEMRA
○ **Activation status**	○ $CD39^+$/$ICOS^+$	CD4_CD39/ICOS
• **$CD8^+$ T cells**	• $CD8^+$, $CD4^-$	CD8
○ **Naïve**	○ $CD45RA^+$, $CCR7^+$	CD8_Naive
○ **Central memory**	○ $CD45RA^-$, $CCR7^+$	CD8_CM
○ **Effector memory**	○ $CD45RA^-$, $CCR7^-$	CD8_EM
○ **TEMRA**	○ $CD45RA^+$, $CCR7^-$	CD8_TEMRA
○ **Activation status**	○ $CD39^+$/$ICOS^+$	CD8_CD39/ICOS

Supplementary Table 4: Patients with irAE

ID	Age	Sex	Tumour Type	Treatment	Type of irAE	Grade	Time to irAE development (weeks)	Treatment
ICB004	37	M	RCC	Nivolumab	Pneumonitis	3°	55	2,0 mg/kg/d prednisone
ICB005	82	M	RCC	Nivolumab	Prurigo nodularis	1°-2°	12	Topical steroids
ICB006	62	F	RCC	Nivolumab	Prurigo	1°	17	Antihistamines
ICB010	35	F	RCC	Nivolumab	Exacerbation of ulcerative colitis	3°	10	Vedolizumab/ 1 mg/kg/d prednisone
ICB011	65	M	RCC	Ipilimumab/ Nivolumab	Dermatitis	2°	1	0,75 mg/kg/d prednisone
					Colitis	3°	12	1,5 mg/kg/d prednisone
ICB018	47	M	RCC	Nivolumab	Nephritis	3°	8	1,5 mg/kg/d prednisone
ICB024	63	M	RCC	Nivolumab	Pneumonitis	3°	42	2,0 mg/kg/d prednisone
ICB033	73	M	HNSCC	Nivolumab	Enterocolitis	3°	32	1,5 mg/kg/d prednisone
ICB042	53	M	RCC	Nivolumab	Enterocolitis	1°	12	NA
					Conjunctivitis	1°	14	
					CK increase	1°	17	
					Pancreatitis	1°	20	
ICB046	73	M	HNSCC	Nivolumab	Pneumonitis	3°	11	2,0 mg/kg/d prednisone
ICB051	62	F	Melanoma	Ipilimumab/ Nivolumab	Myositis	3°	14	2,0 mg/kg/d prednisone
					Pneumonitis	2°		
					Hepatitis	2°		
					Dermatitis	1°		
					Thyroiditis	2°		
ICB061	55	M	CUP	Pembro	Myositis/ Myocarditis	1°-2°	52	0,5 mg/kg/d prednisone
ICB065	72	F	HNSCC	Pembro	Arthritis	1°	11	NA

Tab S4: Overview of irAE-affected patients. Characteristics of patients affected by severe irAE requiring therapy discontinuation and application of immunosuppressive agents in the course of ICB treatment. *Grades of irAE were determined according to to the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE; version 5.0). NA, not applicable (no treatment given).

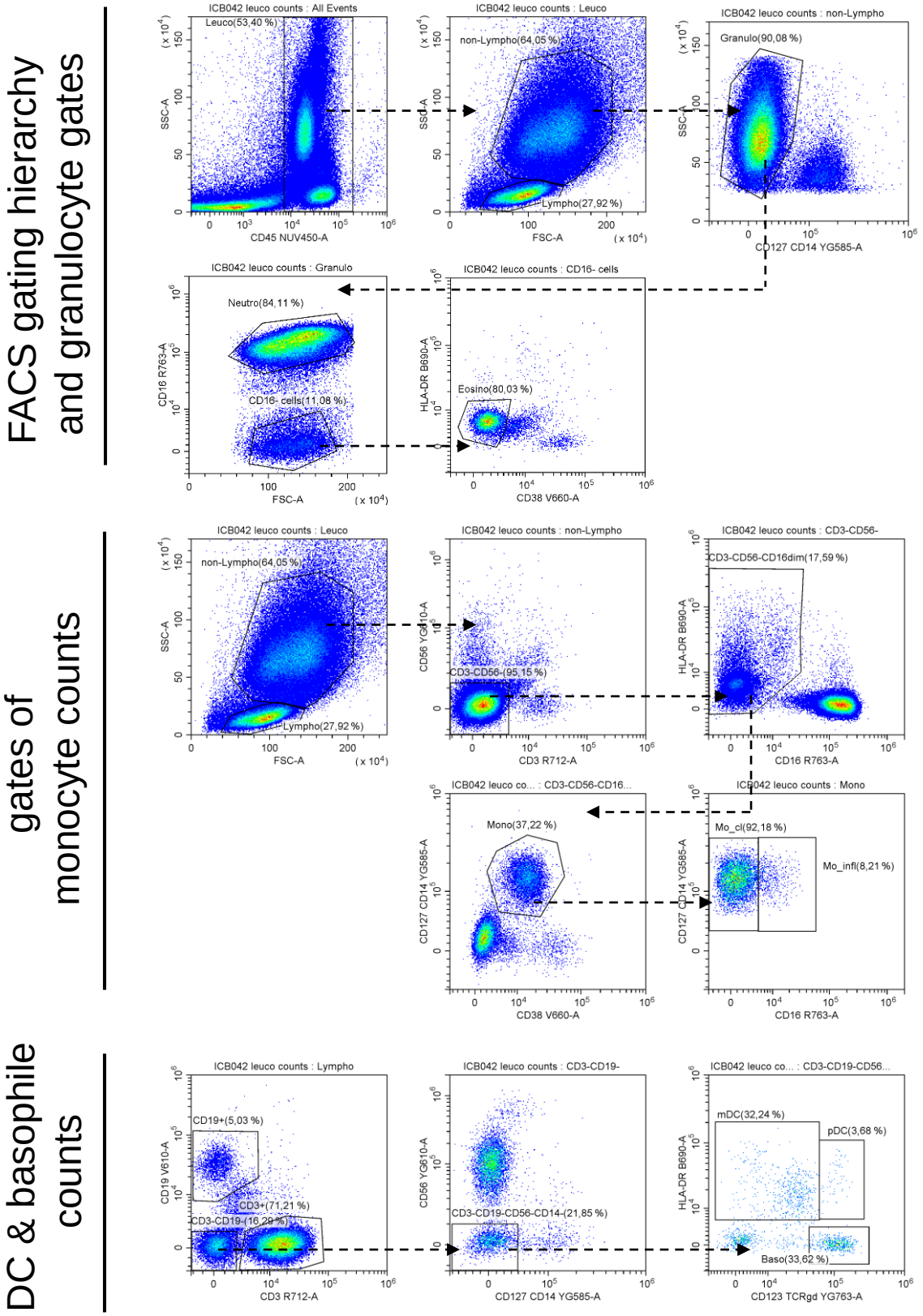
Supplementary Table 5: List of antibodies used

		Antibody	Fluorochrome	Clone	Company
Functional assay	T cell samples	CCR7*	Pe	G043H7	Biolegend
		CD3	A700	UCHT1	Biolegend
		CD40L	BV421	24-31	Biolegend
		IFNγ	Pe/Cy7	B27	BD
		IL-2	APC	N7.48 A	Miltenyi
		CD4	BV605	RPA-T4	Biolegend
		CD8	PerCP	SK1	Biolegend
		TNFα	FITC	MAb11	Biolegend
		CD45RA*	BV785	HI100	Biolegend
		IL10	Pe/Dazzle	JES3-19F1	Biolegend
		IL17	APC/Cy7	BL168	Biolegend
	B cell samples	CD19	PerCP/Cy5.5	HIB19	Biolegend
		CD38	FITC	HB-7	Biolegend
		CD27*	BV605	O323	Biolegend
		CD83	Pe/Cy7	HB15e	Biolegend
		IgD*	APC	IA6-2	Biolegend
		CD86	BV421	IT2.2	Biolegend
		TNFα	A700	MAb11	Biolegend
		IL-10	Pe	JES3-19F1	Biolegend
		IFNγ*	APC/Cy7	4S.B3	Biolegend
	NK cell samples	CD56	BV605	HCD56	Biolegend
		CD19	BV510	SJ25C1	Biolegend
		CD69	PB	FN50	Biolegend
		Perforin	PE	delta G9	Miltenyi
		TNFα*	PerCP	MAb11	Biolegend
		IFNγ	PE/Cy7	4S.B3	BD
		CCL3*	APC	REA257	Miltenyi
		CD3	A700	UCHT1	Biolegend
	Monocyte and DC samples	CD123	PE/Cy7	6H6	Biolegend
		CD11c	APC/F750	S-HCL-3	Biolegend
		CD16	BV605	3G8	Biolegend
		CD56	BV510	5.1H11	Biolegend
		CD19	BV510	SJ25C1	Biolegend
		IL-1b	PB	H1b-98	Biolegend
		TNFα	A700	MAb11	Biolegend
		IL-6	PE	MQ2-13A5	Biolegend
		CD3	BV510	UCHT1	Biolegend
		HLA-DR	APC	L243	Biolegend
		CD14	PerCP	HCD14	Biolegend
		IL-10	PeDazzle	JES3-19F1	Biolegend
Whole blood cell count panel		CD25	APC	M-A251	Biolegend
		CD16	APC/F750	3G8	Biolegend
		CD4	BV510	RPA-T4	Biolegend
		CD127	PE	A019D5	Biolegend
		TCRγδ	PE/Cy7	B1	Biolegend
		HLA-DR	PerCP	L243	Biolegend
		CD28	BV785	CD28.2	Biolegend
		CD45	BUV395	HI30	BD
		CD3	A700	UCHT1	Biolegend
		CD14	PE	HCD14	Biolegend
		CD56	PE/Dazzle	HCD56	Biolegend
		CD123	Pe/Cy7	6H6	Biolegend
		IgD	FITC	IA6-2	Biolegend
		CD8	A488	SK1	Biolegend
		CD27	BV421	O323	Biolegend
		CD19	BV605	HIB19	Biolegend
		CD38	BV650	HB-7	Biolegend
		CD33*	BV785	WM53	Biolegend
T cell count panel		CD4	BV510	RPA-T4	Biolegend
		CCR7	PE	G043H7	Biolegend
		CD8	PerCP	SK1	Biolegend
		CD3	BUV395	UCHT1	BD
		CD45RA	APC/F750	HI100	Biolegend
		IL-6Ra/CD126*	PE/Cy7	UV4	Biolegend
		CD319*	APC	162.1	Biolegend
		CD31	A700	WM59	Biolegend
		CD39	PE/Dazzle	A1	Biolegend
		PD1/CD279	FITC	EH12.2H7	Biolegend
		ICOS/CD278	BV650	C398.4A	Biolegend

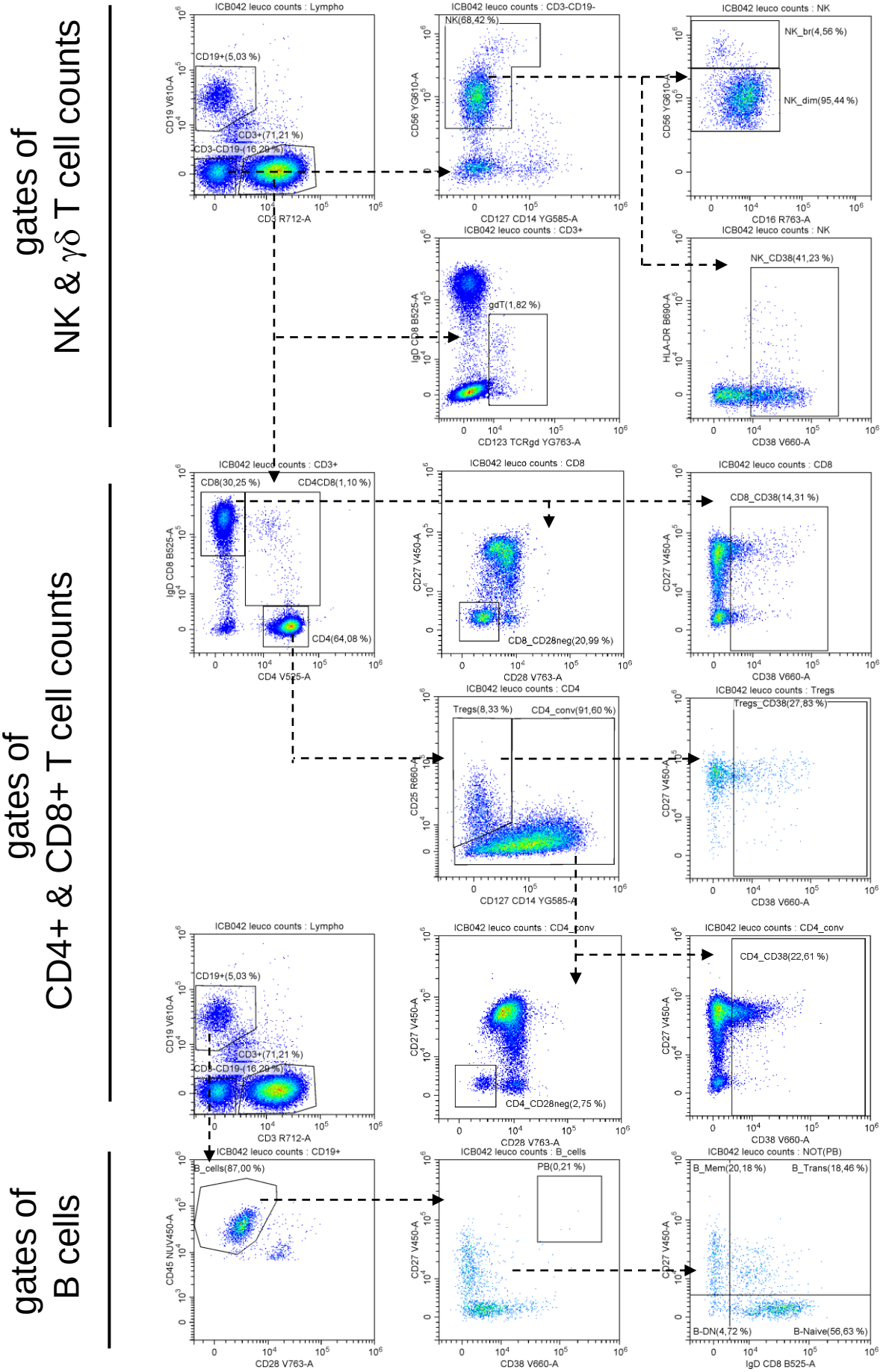
Supplementary Table 6: List of stimulating reagents used

Stimulation reagent	Concentration	Function	Company	Name of product
PEP	1 μg/ml	Pool of 176 peptide epitopes	JPT Peptide Technologies	CEFX Ultra SuperStim Pool
aCD28 Ab	2 μg/ml	Co-stimulation of T cells	BD	Purified NA/LE Mouse Anti-Human CD28
SEB	3 μg/ml	Superantigen	Sigma-Aldrich	Staphylococcal enterotoxin B from Staphylococcus aureus
TSST-1	3 μg/ml	Superantigen	Sigma-Aldrich	Toxic shock syndrome toxin-1 from Staphylococcus aureus
PWM	12.5 μg/ml	TLR4 ligand	Sigma-Aldrich	Lectin from Phytolacca americana (pokeweed)
PMA	30 ng/ml	PKC activator	Sigma-Aldrich	Phorbol 12-myristate 13-acetate
Ionomycin	1 μg/ml	Calcium ionophore	Sigma-Aldrich	Ionomycin calcium salt from Streptomyces conglobatus
mCD40L	3 μg/ml	CD40 ligand	Miltenyi	Human CD40-Ligand Multimer Kits
pHrodo	30 μg/ml	TLR2 ligand	Life Technologies GmbH	pHrodo™ Green Zymosan Bioparticles™ Conjugate for Phagocytosis
PGN	1 μg/ml	NOD2 receptor ligand	InvivoGen	PGN-SA peptidoglycan preparation
IL-12	25 ng/ml	IL-12	Miltenyi	Human IL-12
IL-15	50 ng/ml	IL-15	Miltenyi	Human IL-15
IL-18	100 ng/ml	IL-18	Biolegend	Recombinant Human IL-18 (carrier-free)
ODN	10 μg/ml	TLR9 ligand	Biomol	ODN M362 (Type C) Endotoxin-free (sterile)
R848	1 μg/ml	TLR7/8 ligand	Cayman Chemical	Resiquimod
LPS	100 ng/ml	TLR4 ligand	Sigma-Aldrich	Lipopolysaccharides from Escherichia coli O111:B4

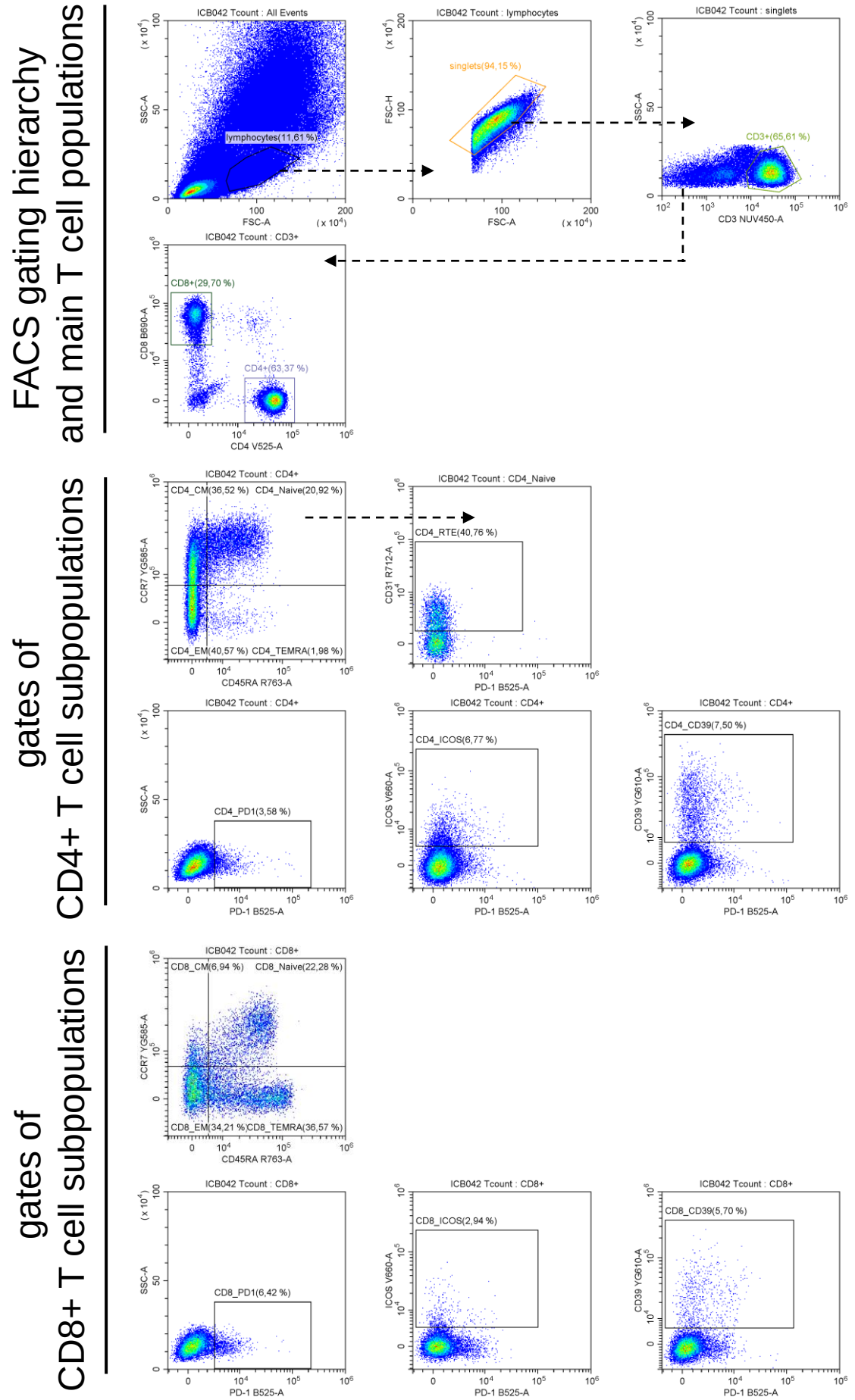
Supplementary Figure 1A: Representative gating strategy of leukocyte counts (non-lymphocyte populations)



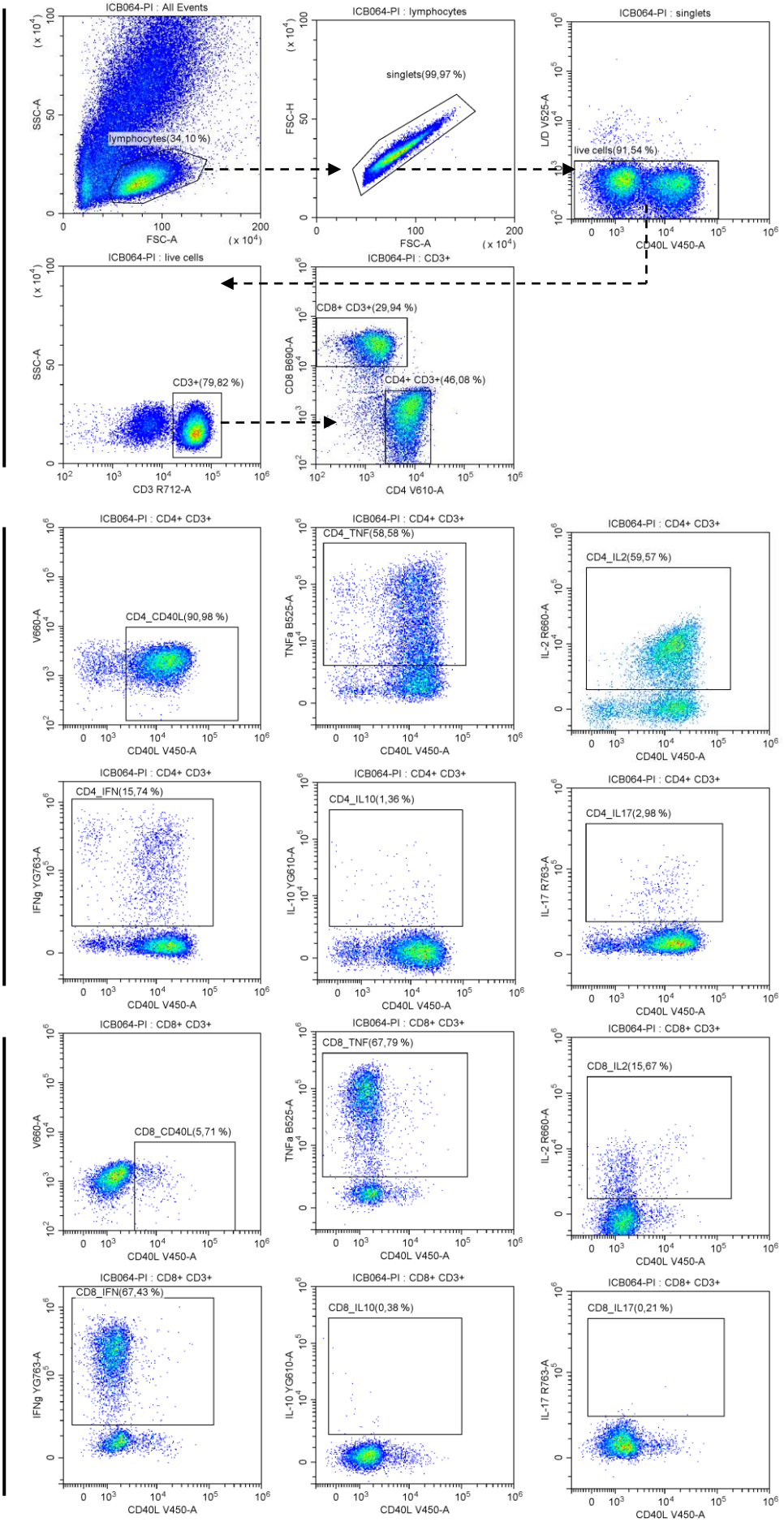
Supplementary Figure 1A: Representative gating of leukocyte counts (lymphocyte populations)



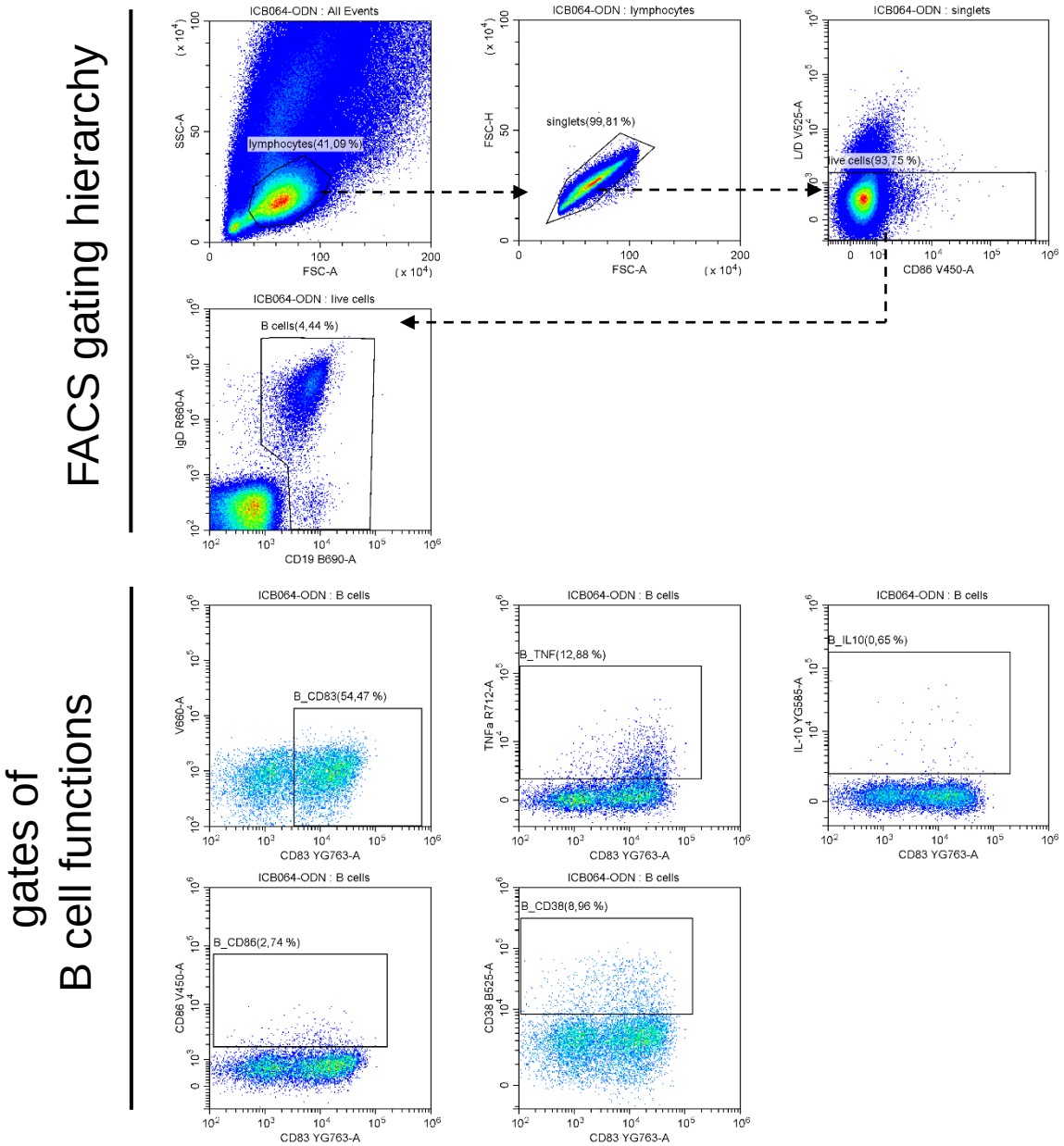
Supplementary Figure 1B: Representative gating of T cell population counts



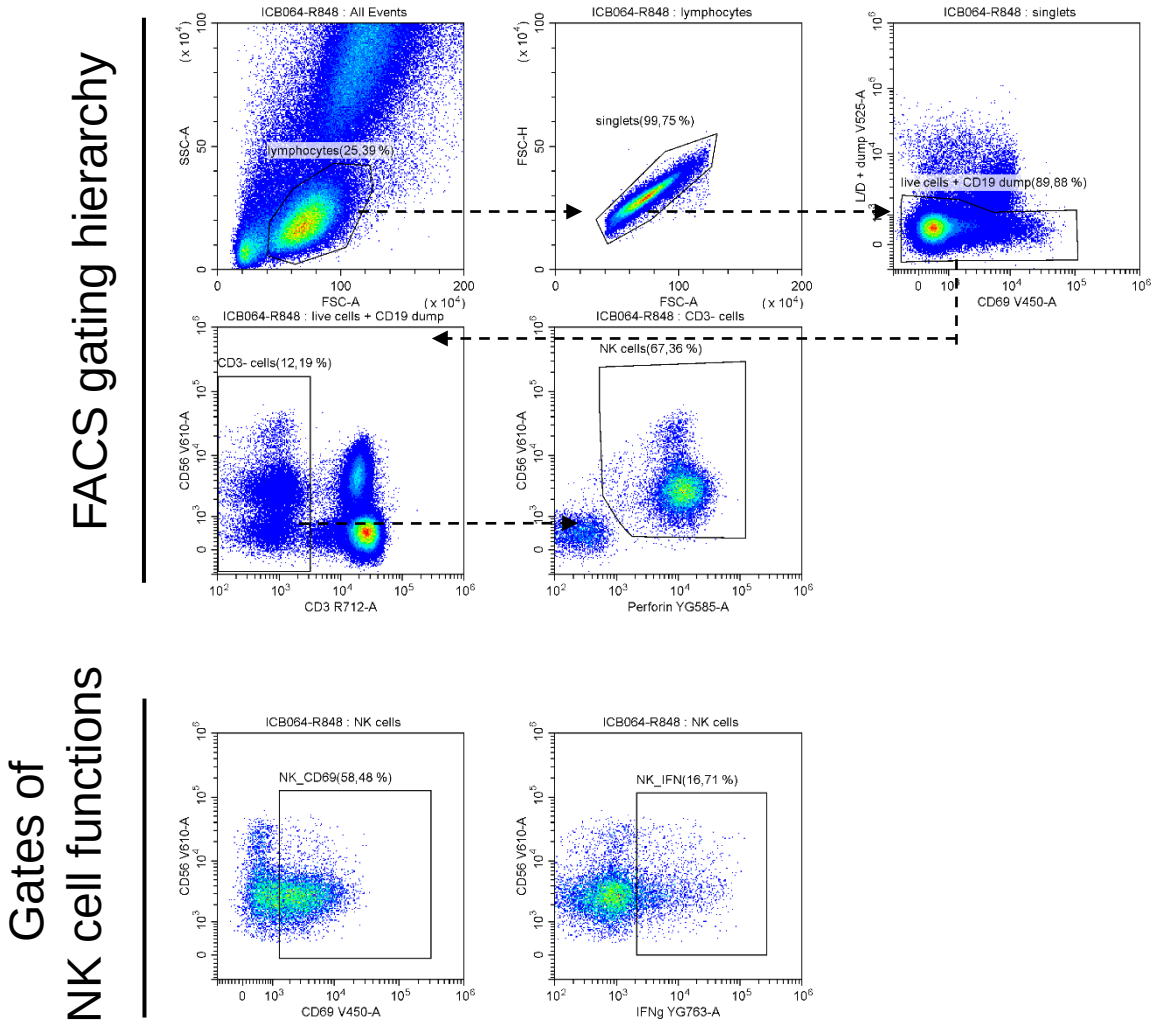
Supplementary Figure 1C: Representative gating of T cell functions



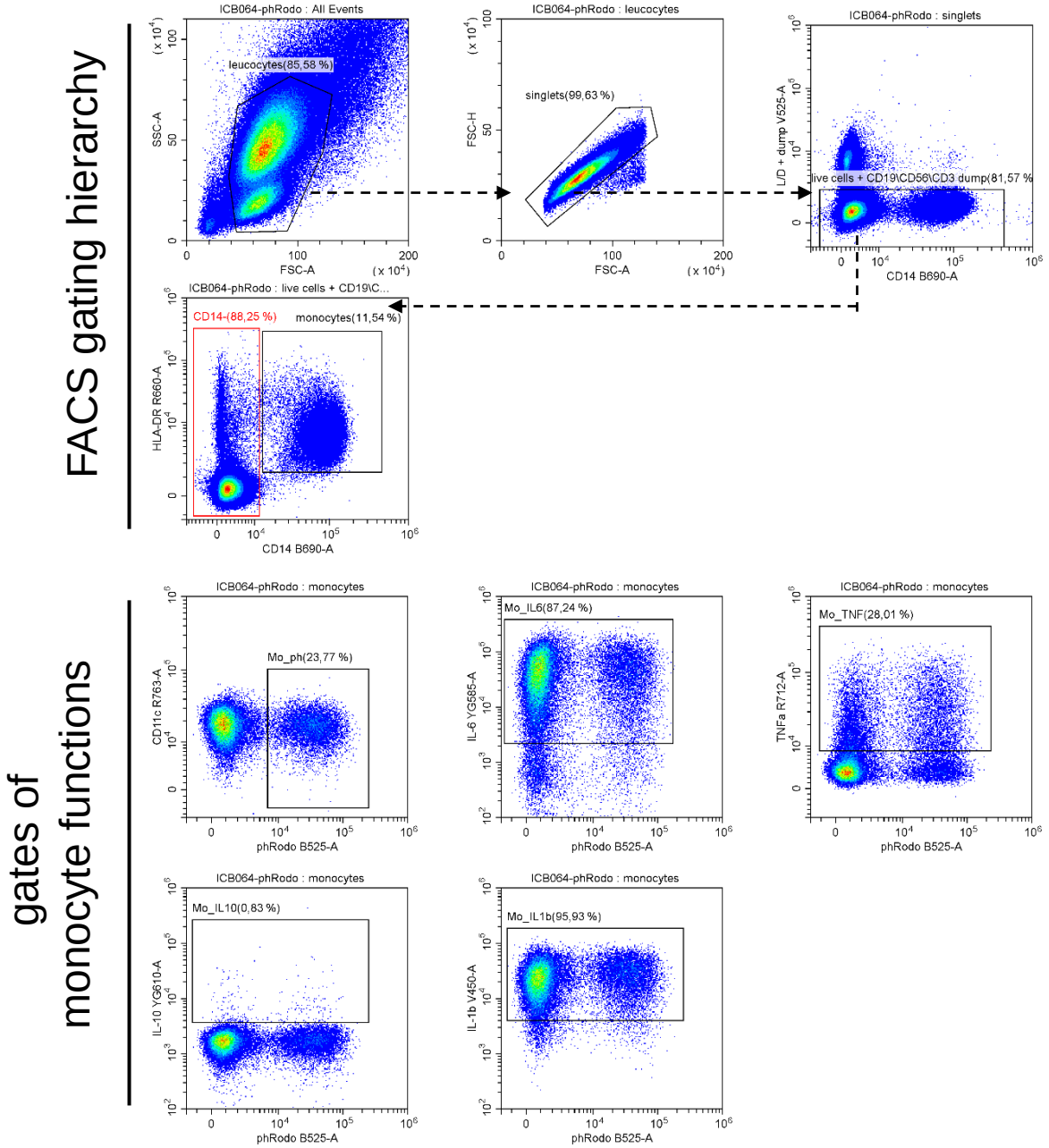
Supplementary Figure 1D: Representative gating of B cell functions



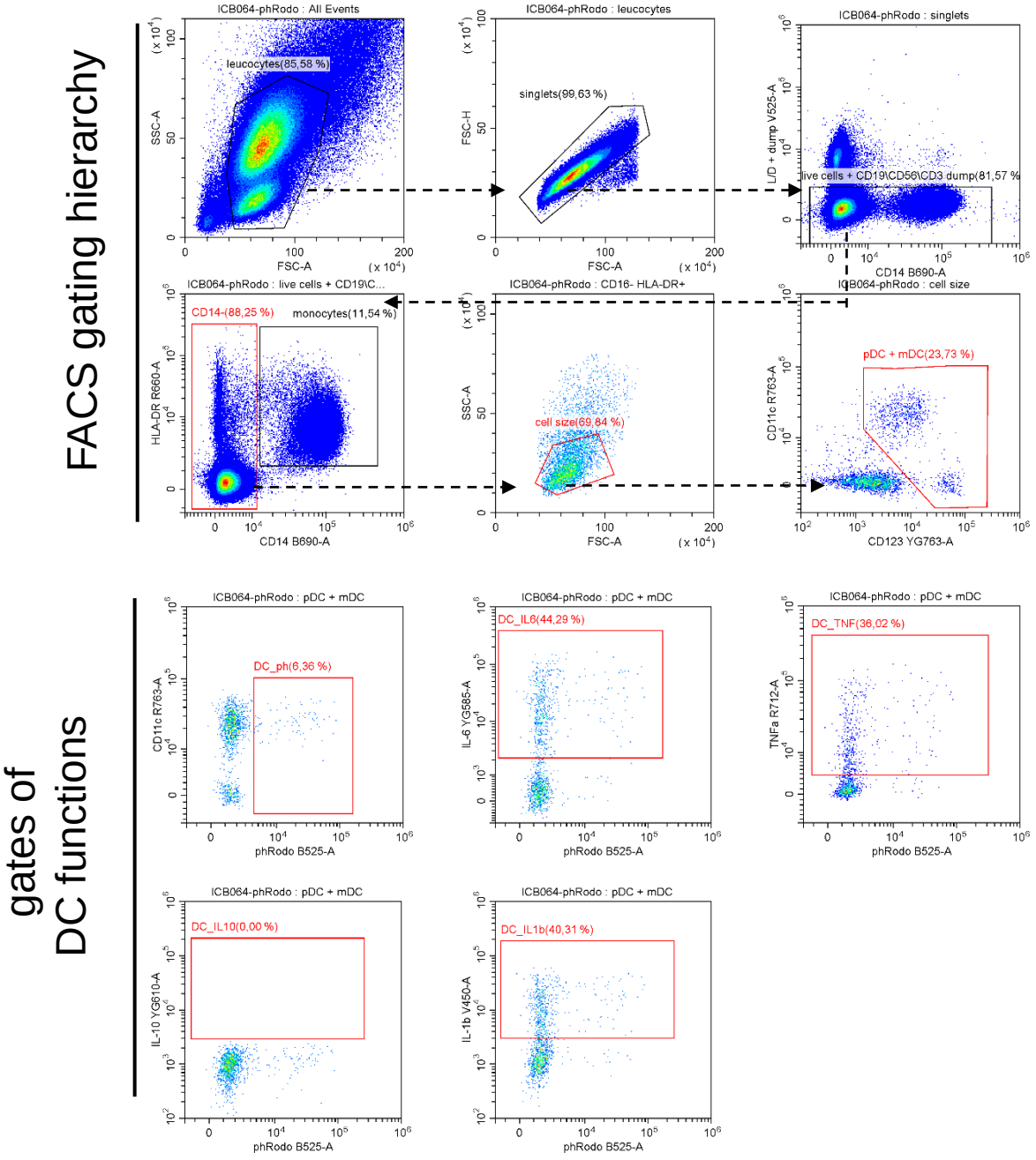
Supplementary Figure 1E: Representative gating of NK cell functions



Supplementary Figure 1F: Representative gating of monocyte functions



Supplementary Figure 1G: Representative gating of DC functions



Supplementary Figure 2

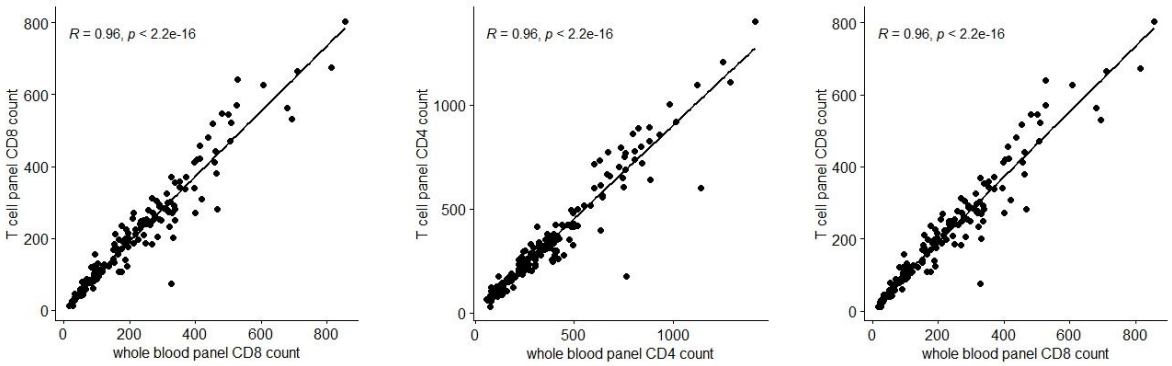


Fig. S2: Correlation of count parameters measured by the leukocyte and T cell panel. Diagrams display the count value obtained with two independent flow cytometric measurements. Statistical analysis: Pearson correlation with linear regression line.

Supplementary Figure 3

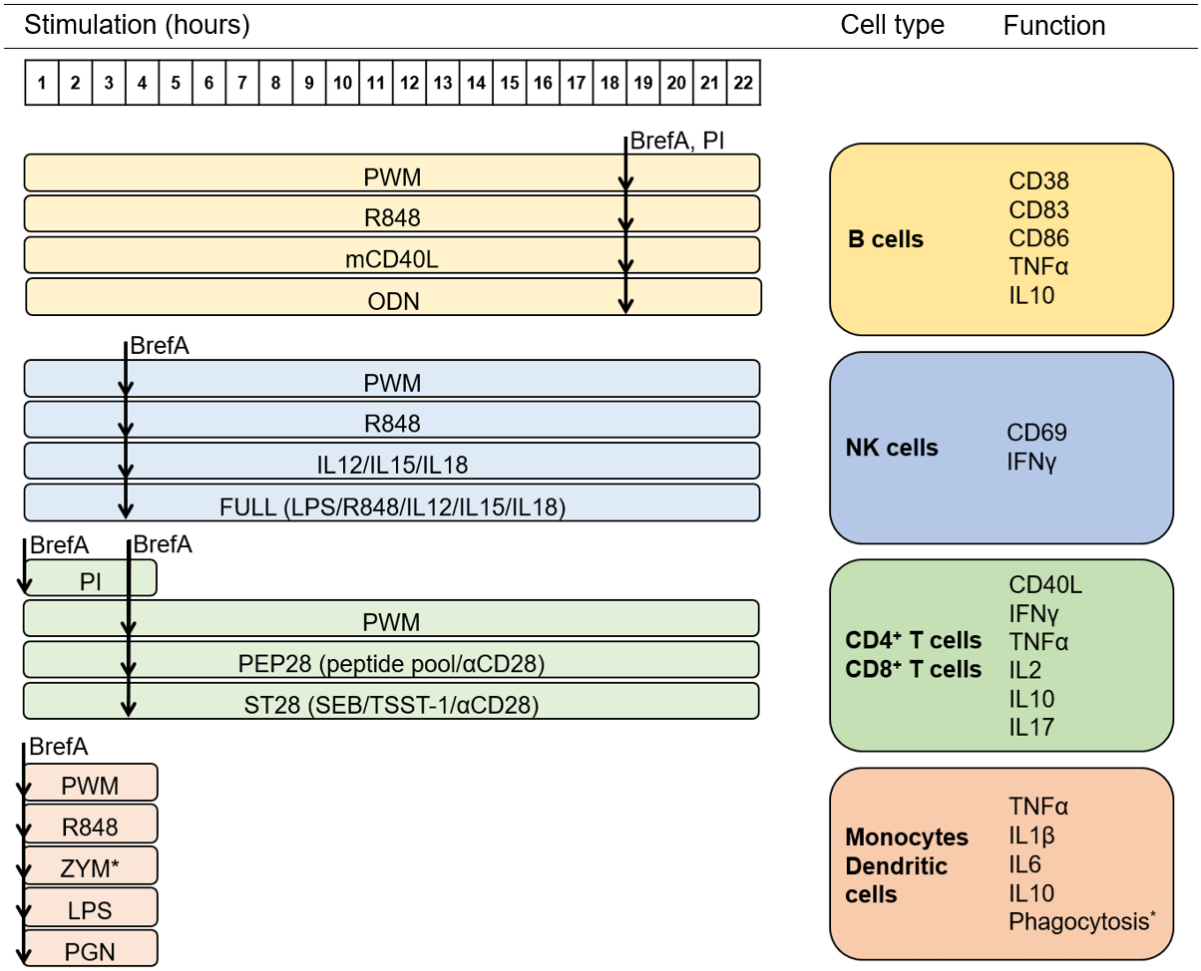


Fig. S3: Overview of the stimulation procedure and measured functional parameters. * For the measurement of phagocytosis activity samples were stimulated with zymosan conjugated with a pH sensitive fluorochrome.

Supplementary Figure 4

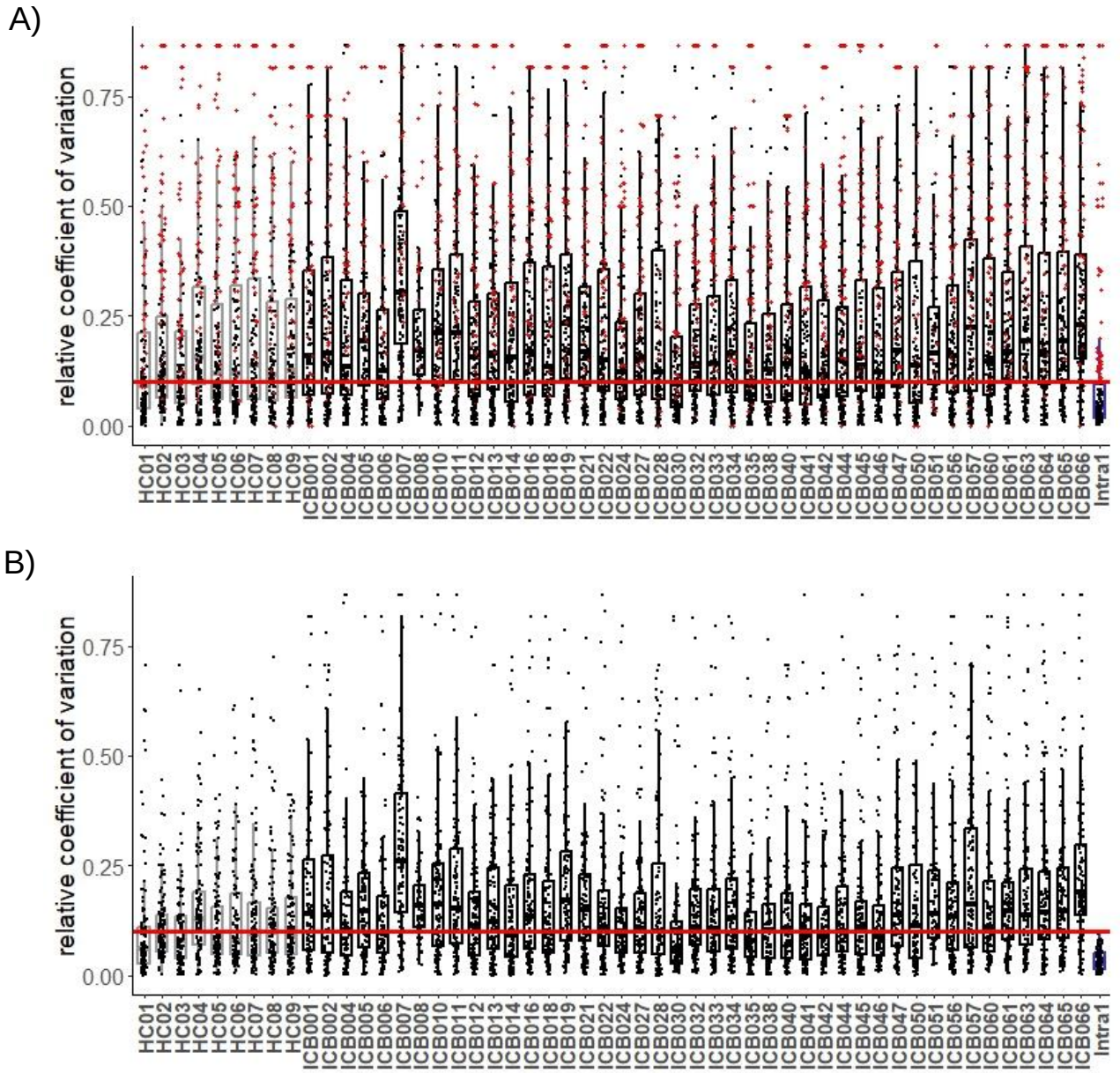


Fig. S4: Parameter selection based on an intra-day variance threshold. In both diagrams the variance across the four visits is plotted for each parameter and donor. Each dot represents a parameter. For a better discrimination Box-Whisker charts are overlaid. All parameters with relative coefficient of variance above 10% in intra-day experiment performed in quadruplicate at the same day were excluded by the subsequent analysis (donor = Intra 1). The 10% threshold is marked with a red horizontal line and (**A**) in the upper diagram the excluded parameters are visualized in all donors as red dots. (**B**) In the lower diagram these parameters and accordingly the Box-Whisker charts and the median of the relative coefficient of variation per donor are changed. The medians after filtering were used for the variance comparison in Fig. 3A.

Supplementary Figure 5

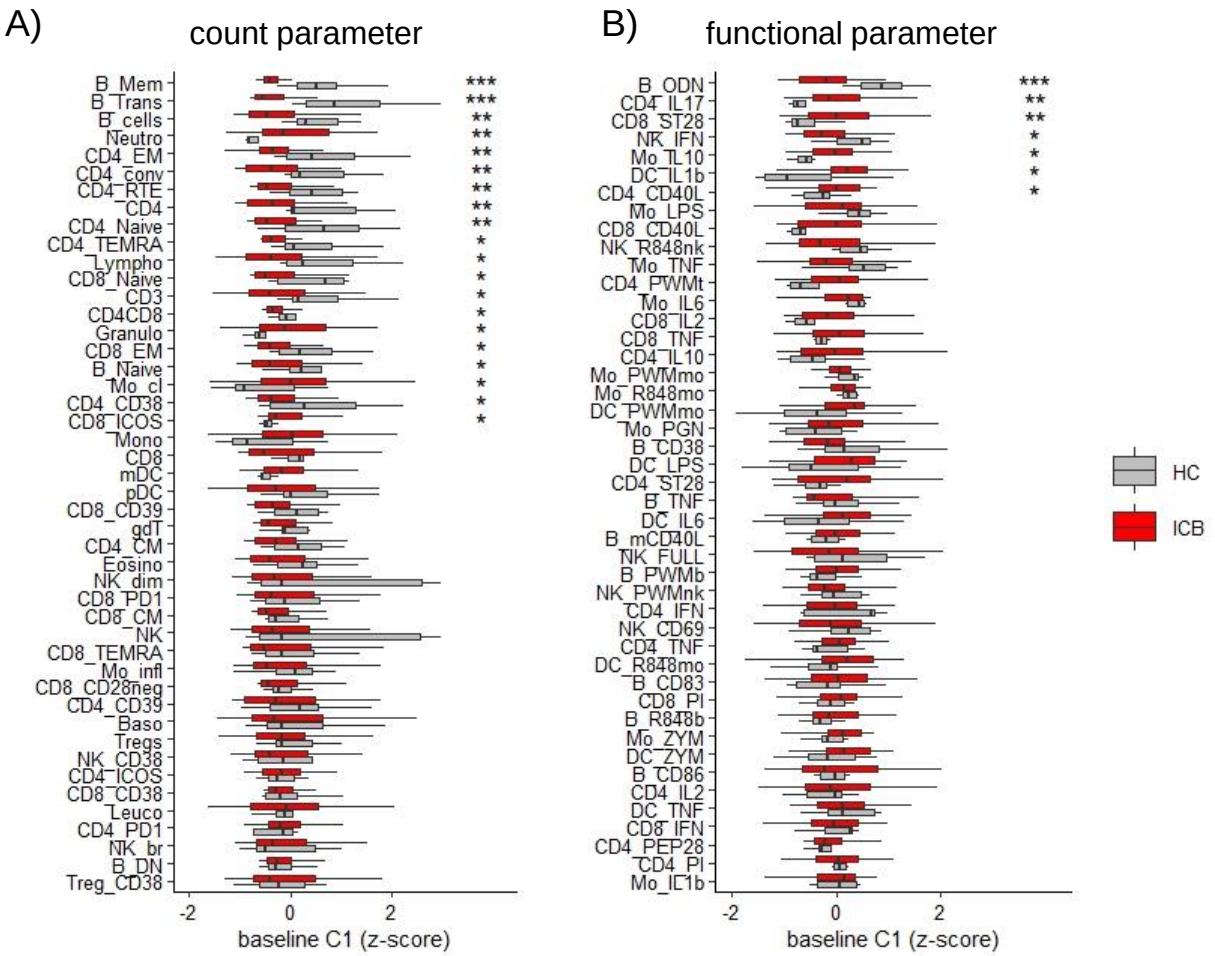


Fig. S5: Quantitative and functional immune conditions at baseline in HC (n=9) and ICB patients (n=43). (**A**) Box-Whisker plots of all count parameters and (**B**) all pooled functional parameters comparing HC and cancer patients are displayed with respective p values. Statistical analysis: (**A-B**) Mann-Whitney test.

Supplementary Figure 6:

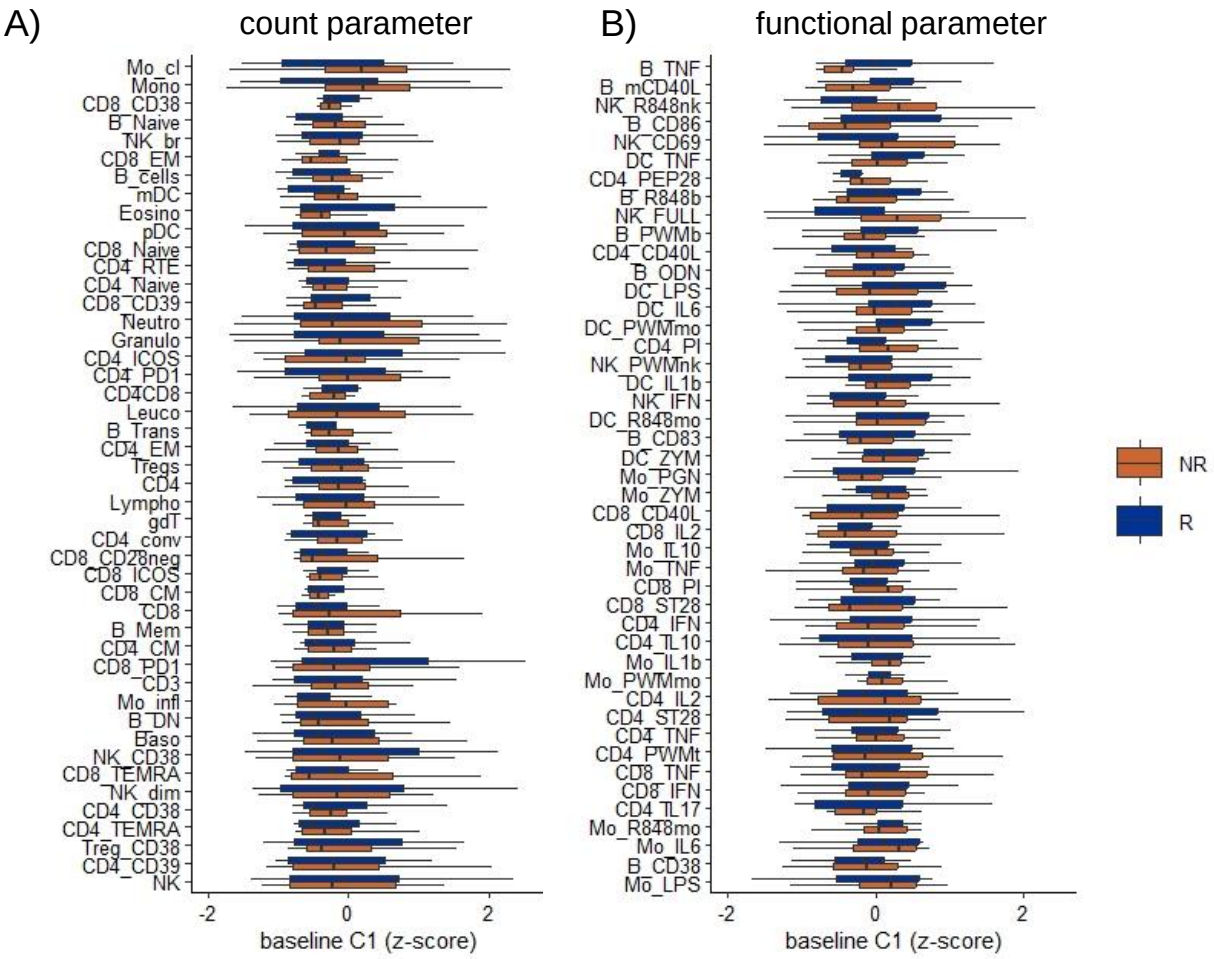


Fig. S6: Quantitative and functional immune conditions at baseline in patients grouped by therapy response in responder (R, n=17) and non-responder (NR, n=18). (**A**) Box-Whisker plots of all count parameters and (**B**) all pooled functional parameters comparing R and NR are displayed with related p values. Statistical analysis: Mann-Whitney test.

Supplementary Figure 7:

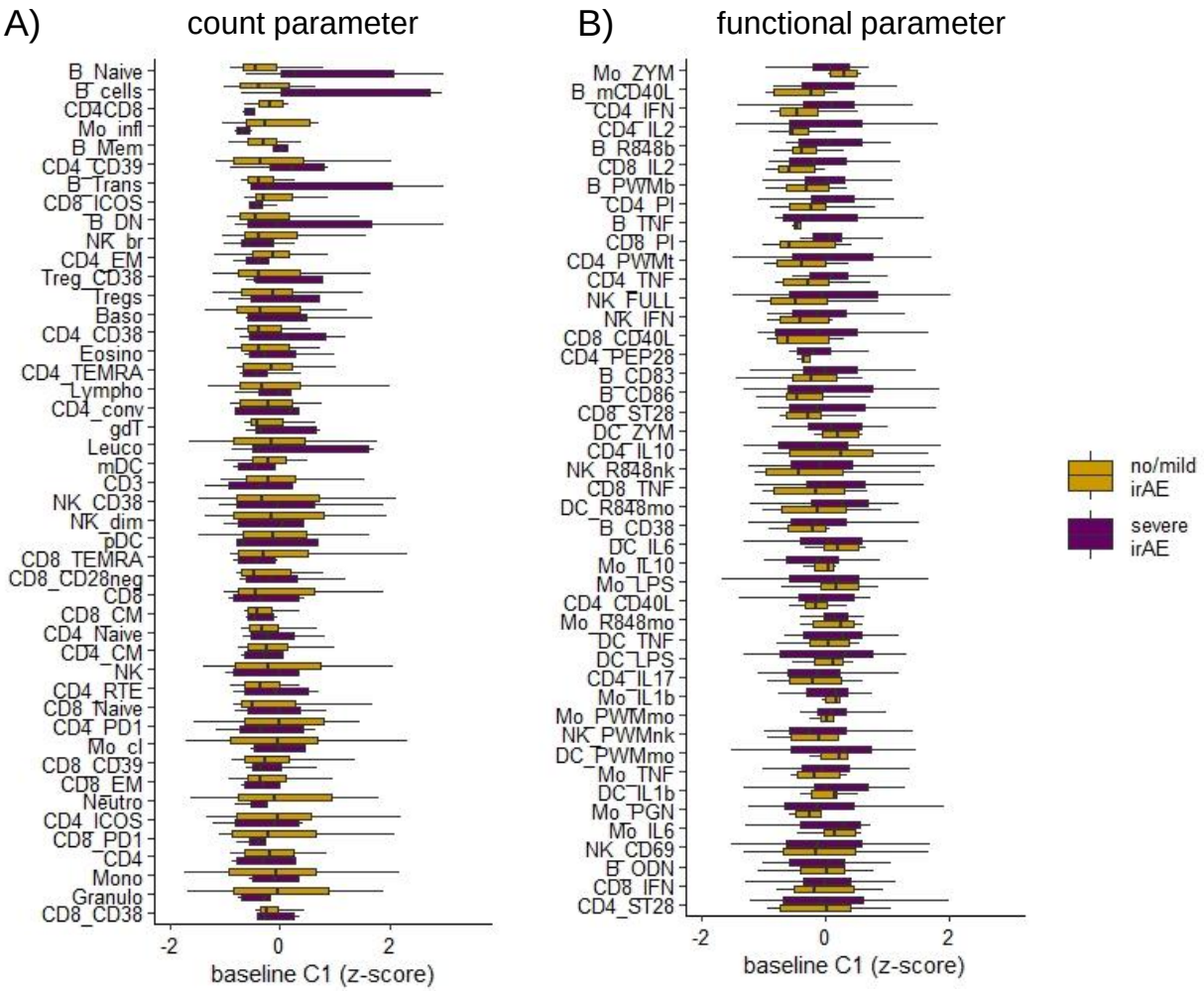


Fig. S7: Quantitative and functional immune conditions at baseline in patients who developed severe irAE (n=6) compared to those who did not (no/mild irAE; n=29) (**A**) Box-Whisker plots of all count parameters and (**B**) all pooled functional parameters comparing irAE and non-irAE patients are displayed with related p values. Statistical analysis: Mann-Whitney test.

Supplementary Figure 8:

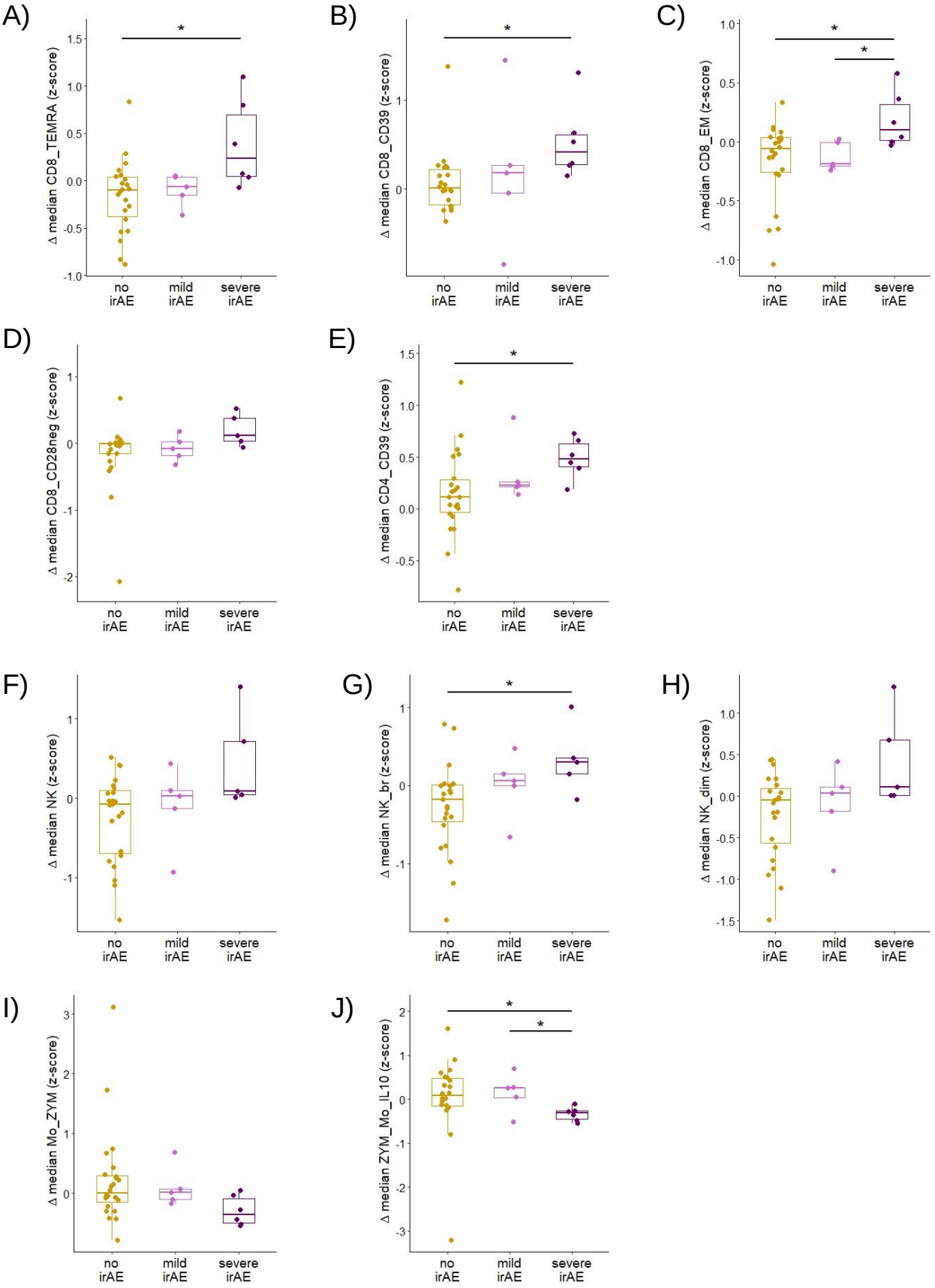


Fig. S8: Comparison of immune dynamics during PD1 blockade therapy in patients with no/mild/severe irAE. Only the significant count parameters from Fig. 3C-3E are presented. Statistical analysis: Kruskal-Wallis test with Dunn's multiple comparisons post-hoc test and Benjamini-Hochberg p value adjustment; $p < 0.05$ = *