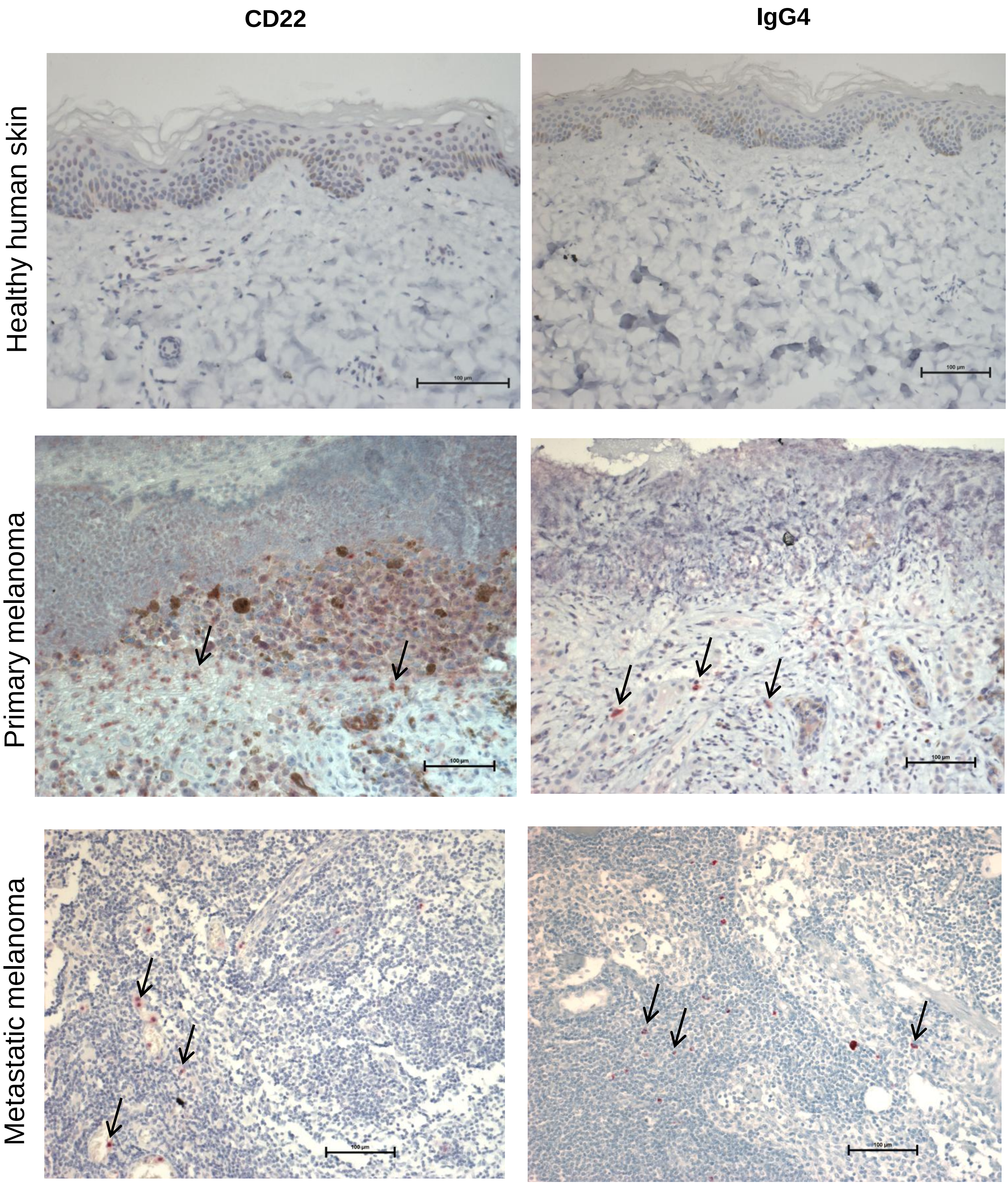
Supplementary Figure 1



Supplementary Figure 1: Immunohisochemical analysis of CD22+ (left) and IgG4 (right), cells (shown in red and indicated by arrows) in healthy skin, primary and metastatic melanoma lesions. Counterstaining in hematoxylin (blue; Scale bar: 100 µm, magnification 10x).

Supplementary Figure 2

A

FR-1 CDR-1

GAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTCAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCATCTATGCCATGAGCTGGG

FR-2 CDR-2

TCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAACTATTAGTGGTAGTGCTGATAGCACATACTACGCAGACTCCGTGAAGGGCCGCTTCACCATCTCCAGAGA

FR-3 CDR-3

CAACTCCAAGAACACGCTGTATTTGCAAATGAACAGCCTGAGAACTGAGGACACGGCTGTGTATTACTGTGCGAAAGGGACACTGGCTACGAAGGGCGGTATGGACGTC

FR-4

TGGGGCCAAGGGACCACGGTCACCGTCTCCTCA

B

	GCC	TCC	ACC	AAG	GGC	CCA	TCC	GTC	TTC	CCC	CTG	GCG	CCC	TGC	TCC	AGG	AGC	ACC	TCC	GAG	AGC	ACA	GCC	GCC	CTG	GGC	TGC
M173	A	S	T	K	G	P	S	V	F	P	L	A	P	C	S	R	S	T	S	E	S	T	A	A	L	G	C
K01316	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
P01861	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

γ4

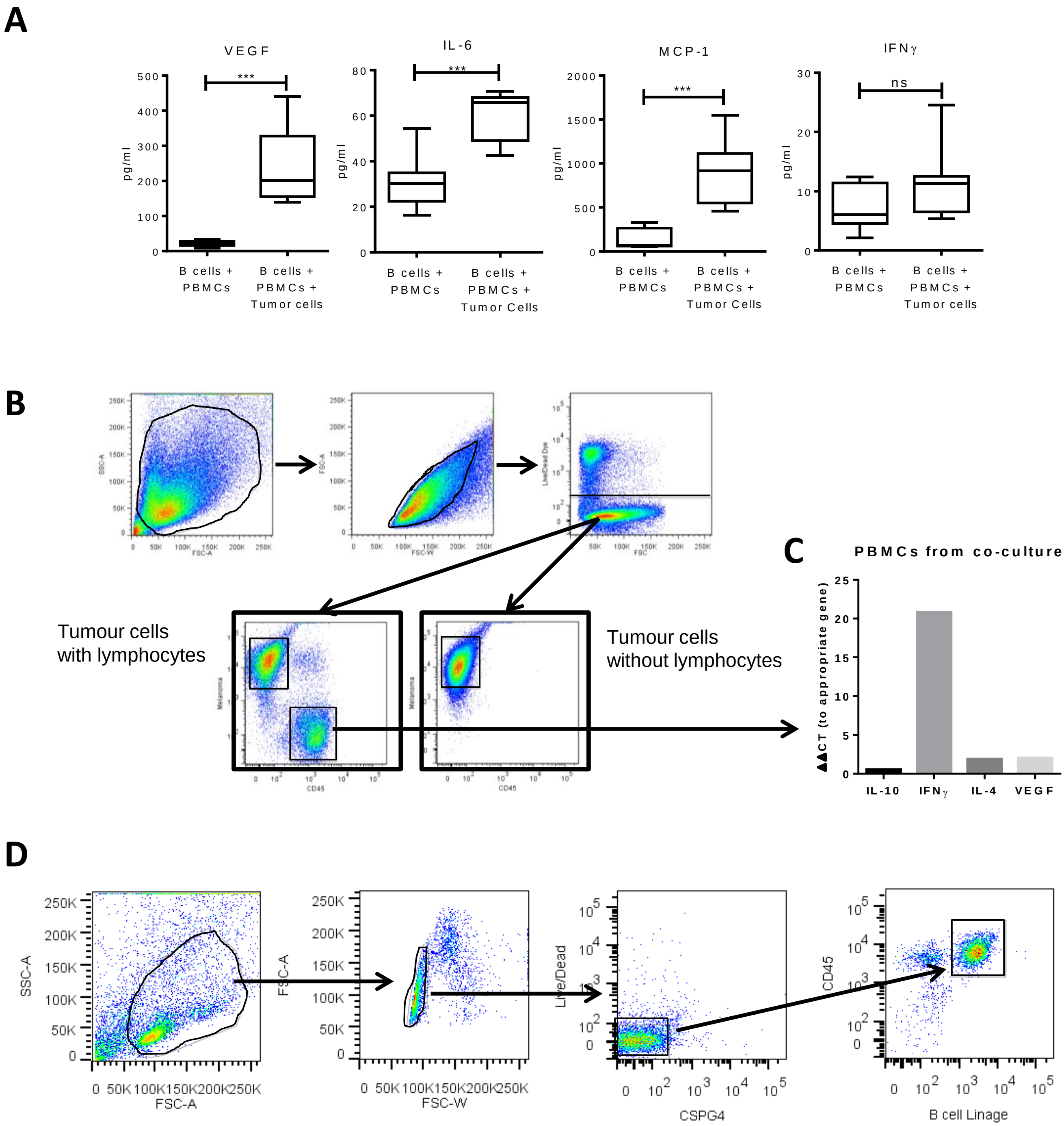
	CTG	GTC	AAG	GAC	TAC	TTC	CCC	GAA	CCG	GTG	ACG	GTG	TCG	TGG	AAC	TCA	GGC	GCC	CTG	ACC	AGC	GGC	GTG	CAC	ACC	TTC	CCG
M173	L	V	K	D	Y	F	P	I	P	V	T	V	S	W	N	S	G	A	L	T	S	G	V	H	T	F	P
K01316	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
P01861	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

	GCT	GTC	CTA	CAG	TCC	TCA	GGA	CTC	TAC	TCC	CTC	AGC	AGC	GTG	GTG	ACC	GTG	CCC	TCC	AGC	AGC	TTG	GGC	ACC	CAG	ACC	TAC
M173	A	V	L	Q	S	S	G	L	Y	S	L	S	S	V	V	T	V	P	S	S	S	L	G	T	Q	T	Y
K01316	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	K	-	-
P01861	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	K	-	-

	ATC	TGC	AAC	GTG	AAT	CAC	AAG	CCC	AGC	AAC	ACC	AAG	GTG	GAC	AAG	AGA	GTT
M173	I	C	N	V	N	H	K	P	S	N	T	K	V	D	K	R	V
K01316	T	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
P01861	T	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

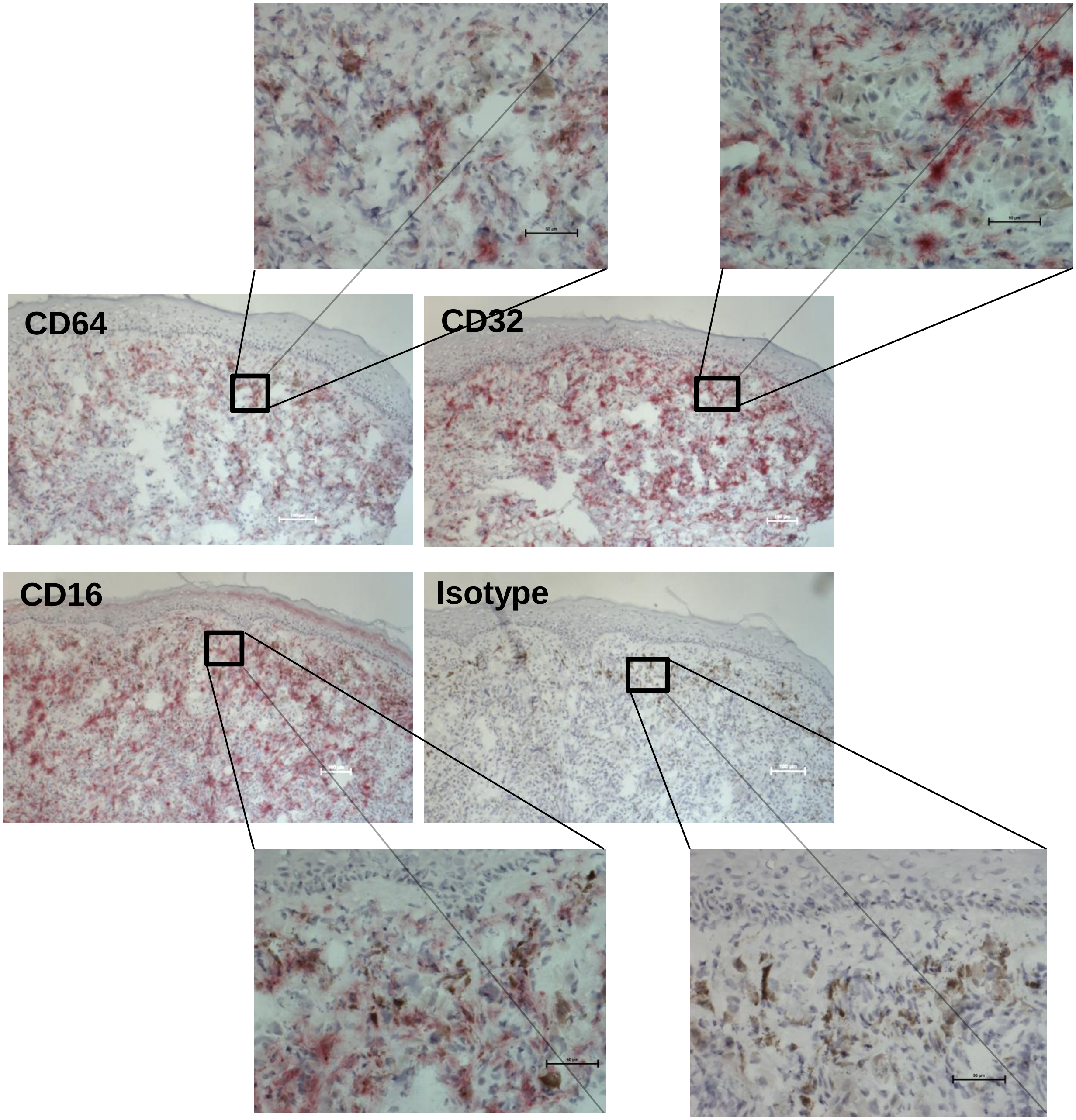
Supplementary Figure 2: V_H-D-J (**A**) and alignment of γ4 constant region (**B**) amplified by RT-PCR from a melanoma patient (M173) indicating that the acquired protein sequence has the highest similarity with IGHG4 (Accession P01861;K01316) analysed using Blast/Uniport (http://www.uniprot.org/blast/uniprot).

Supplementary Figure 3



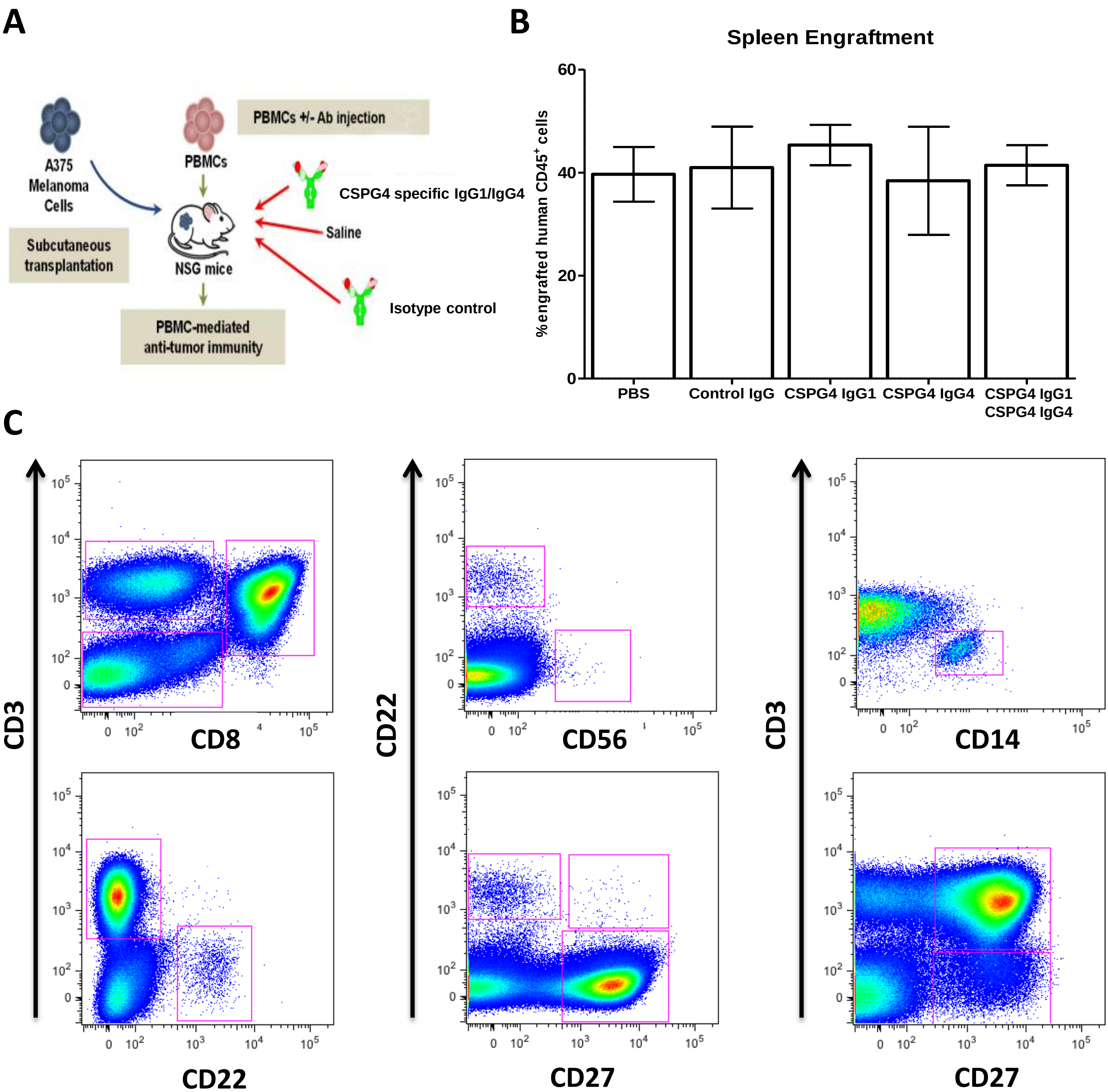
Supplementary Figure 3: (A) Cytokines secreted in culture supernatants of B cells and PBMCs stimulated with or without A375 melanoma tumour cells were analysed by Luminex bead array analysis. Titres of VEGF, IL-6 and MCP-1, but not of IFNγ, were significantly increased in cultures treated with tumour cells (*** $P<0.001$; ns = not significant $P>0.05$, analysed by using Mann-Withney-U-test, n=9). **(B)** Flow cytometric sorting strategy to isolate A375 tumor cells and PBMCs from co-culture experiments; purified cells were used to examine cytokine expression in Figure 3D and expression of cytokines by PBMC in these cultures is depicted in **(C)**. **(D)** Flow cytometric sorting strategy to isolate B cells from co-culture experiments described in Figure 3F.

Supplementary Figure 4



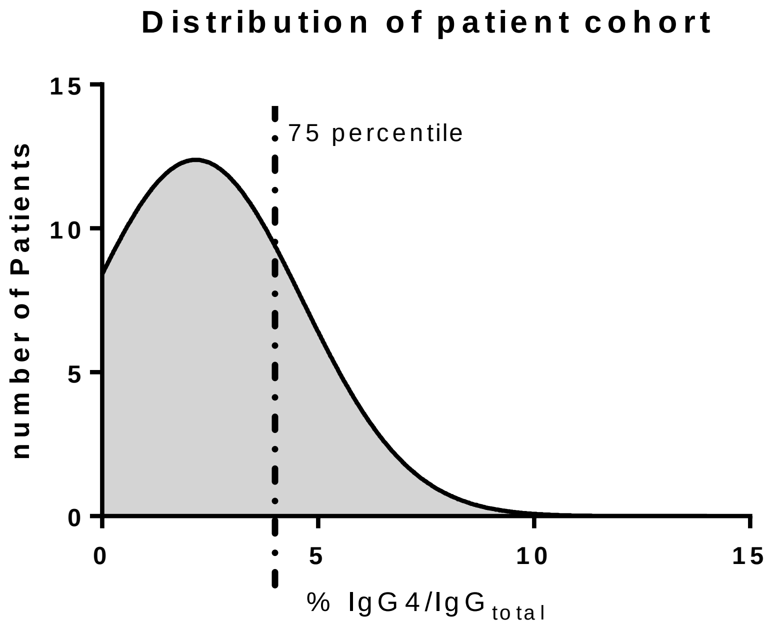
Supplementary Figure 4: Immunohistochemical analysis of FcγR distribution was conducted using fresh-frozen sections of human melanoma lesions and visualized using AP (in red). Representative images demonstrate all three families of FcγRs, i.e. FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) widely expressed in melanoma lesions. Main images were captured at 10x magnification (scale bars: 100 μm); magnified images were captured at 20x (scale bars: 50 μm).

Supplementary Figure 5



Supplementary Figure 5: (A) Design of in vivo model in NOD/scid/ IL-2Rγ$^{-/-}$ mice to determine antibody-mediated effector functions. **(B)** Engraftment of human CD45+ immune cells in mouse spleens, evaluated by flow cytometry showed no significant difference in human CD45^{+} engraftment across treatment groups. **(C)** Representative flow cytometric gating strategies to identify immune cell subsets within the human CD45^{+} mouse CD45^{-} gates engrafted in mouse spleens.

Supplementary Figure 6



Supplementary Figure 6: Patient distribution based on % IgG4\IgG$_{total}$; black dashed line indicates the 75 percentile, used as cut off point for cumulative survival analysis (Figure 8).

Supplementary Table 1: Clinical parameters and disease staging of peripheral blood donors used for ex vivo B cell cultures at the time of sampling (Figures 2 and 3).

Patient ID	Gender	Age	Stage	TNM
M282	F	43	IB	T2a;N0;M0
M285	M	82	IIA	T2b;N0;M0
M286	F	68	IIB	T4a;N0;M0
M287	F	62	IIIA	T2a;N1a;M0
M338	M	72	IIIB	Tx;N2c;M0
M385	M	67	IIIC	Tx;N3;M0
M380	M	41	IIB	T4a;N0;M0
M381	M	57	IB	T1b;N0;M0
M386	F	64	IIIB	Tx;N2c;M0
M394	M	56	IIB	T4a;N0;M0
M396	M	73	IIC	T4b;N0;M0
M397	F	70	IIB	T3b;N0;M0
M401	F	60	IIIA	T2a;N1a;M0
M402	M	50	IIIB	Tx;N1b;M0
M404	F	65	IB	T2b;N0;M0
M405	M	51	IIC	T4b;N0;M0
M408	F	71	IB	T1a;N0;M0
M409	F	78	IIA	T3a;N0;M0
M430	F	78	IIC	T4b;N0;M0
M433	F	48	IIIB	T3b;N2c;M0
M435	M	45	IB	T2a;N0;M0
M437	M	46	IIA	T3a;N0;M0
M438	F	62	IIA	T2b;N0;M0
M443	M	69	IB	T2a;N0;M0
M318	M	60	IB	T2a;N0;M0
M320	F	71	IIB	T3b;N0;M0
M247	F	37	IV	T3b;N0;M1c
M224	F	76	IIB	T3b;N0;M0
M223	M	35	IB	T2a;N0;M0