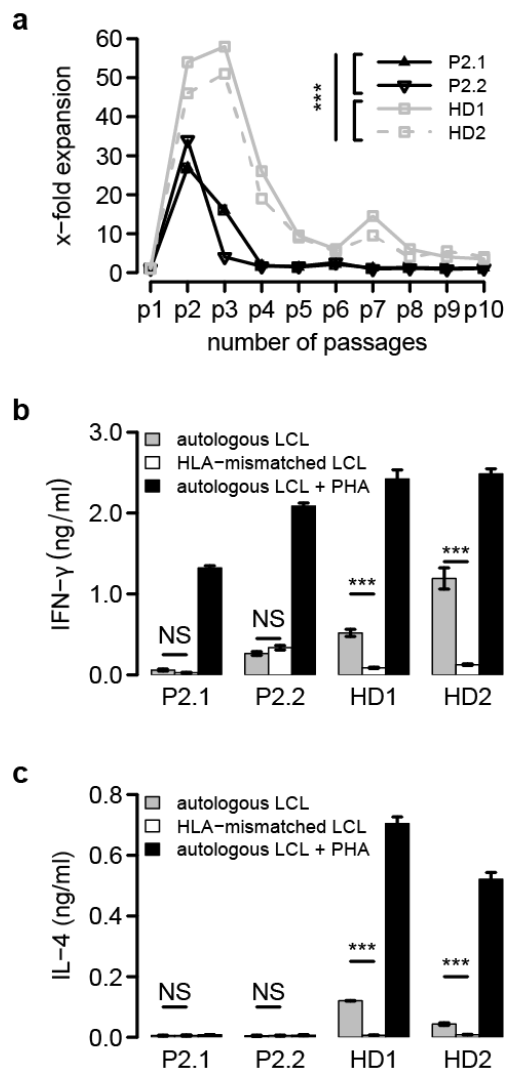
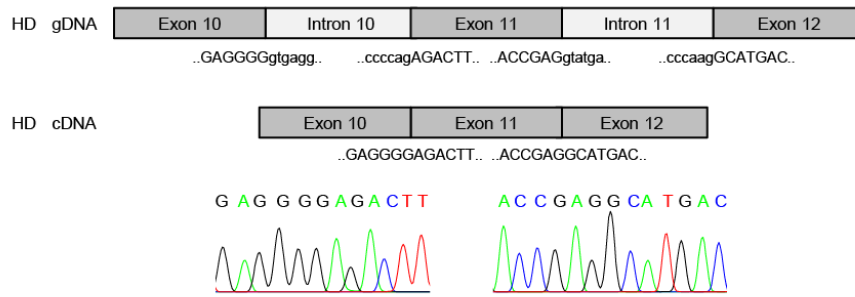


Supplementary Figure 1. EBV⁺ SMT show latency type III. **(a)** P2.1 immunohistochemistry of the EBV proteins LMP1 (negative), LMP2A (scattered positive), EBNA2 (partially positive), ZEBRA (negative), of the EBV B cell entry receptor CD21 (negative), the T cell co-stimulators CD80 and CD86 (negative) and the tumor suppressor P53 (not overexpressed). **(b)** P1.1, P1.2, P2.1 and P2.2 hematoxylin and eosin (H&E) stains with leiomyogenic tumor cells and **(c)** EBER *in situ* hybridization. Scale bars indicate 100 μ m each.

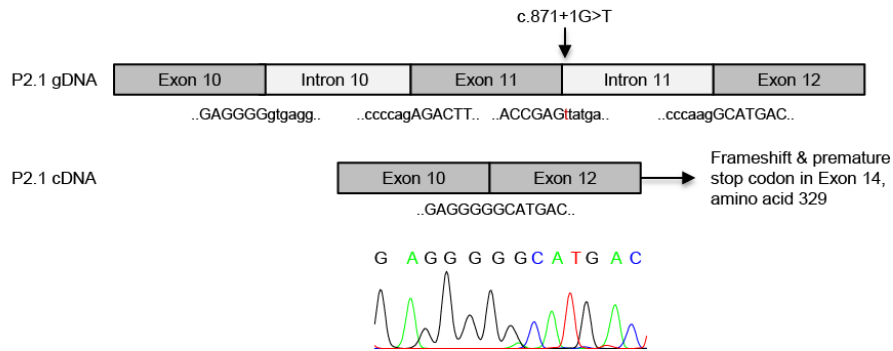


Supplementary Figure 2. CARMIL2-deficient TCL do not respond to autologous EBV⁺ LCL. T cell lines (TCL) from EBV⁺ HD1, HD2, P2.1 and P2.2 were repeatedly stimulated with autologous EBV⁺ lymphoblastoid cell lines (LCL). **(a)** Growth kinetics of TCL over ten passages (p). **(b)** IFN- γ and **(c)** IL-4 secretion of TCL after ten passages upon co-culture with autologous or HLA-mismatched EBV⁺ LCL, or after antigen-independent activation with phytohemagglutinin (PHA). Significance was determined by using two-way ANOVA **(a)**, or the two-tailed unpaired *t*-test analysis **(b)** and **(c)**. Error bars, mean \pm s.e.m. with n=3. NS = non significant. *** $p < 0.0001$.

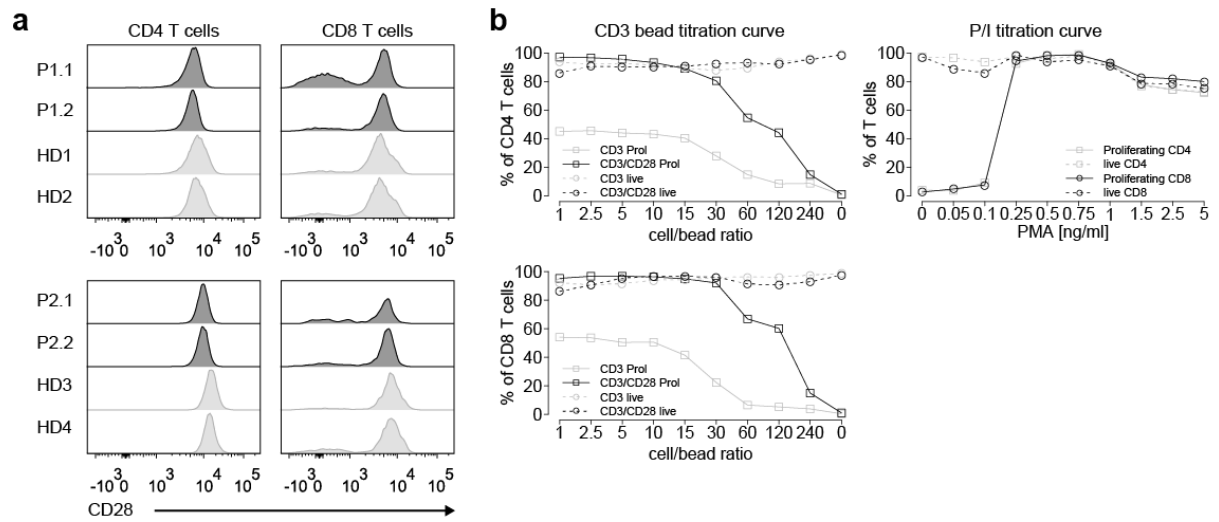
a



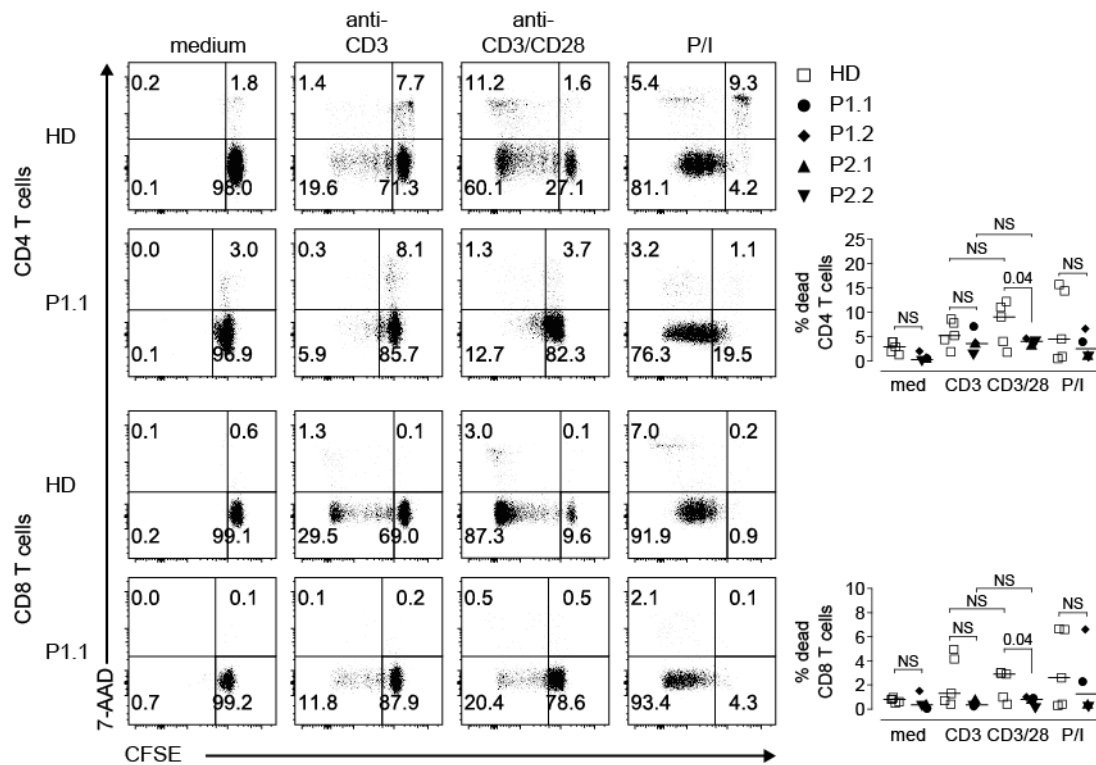
b



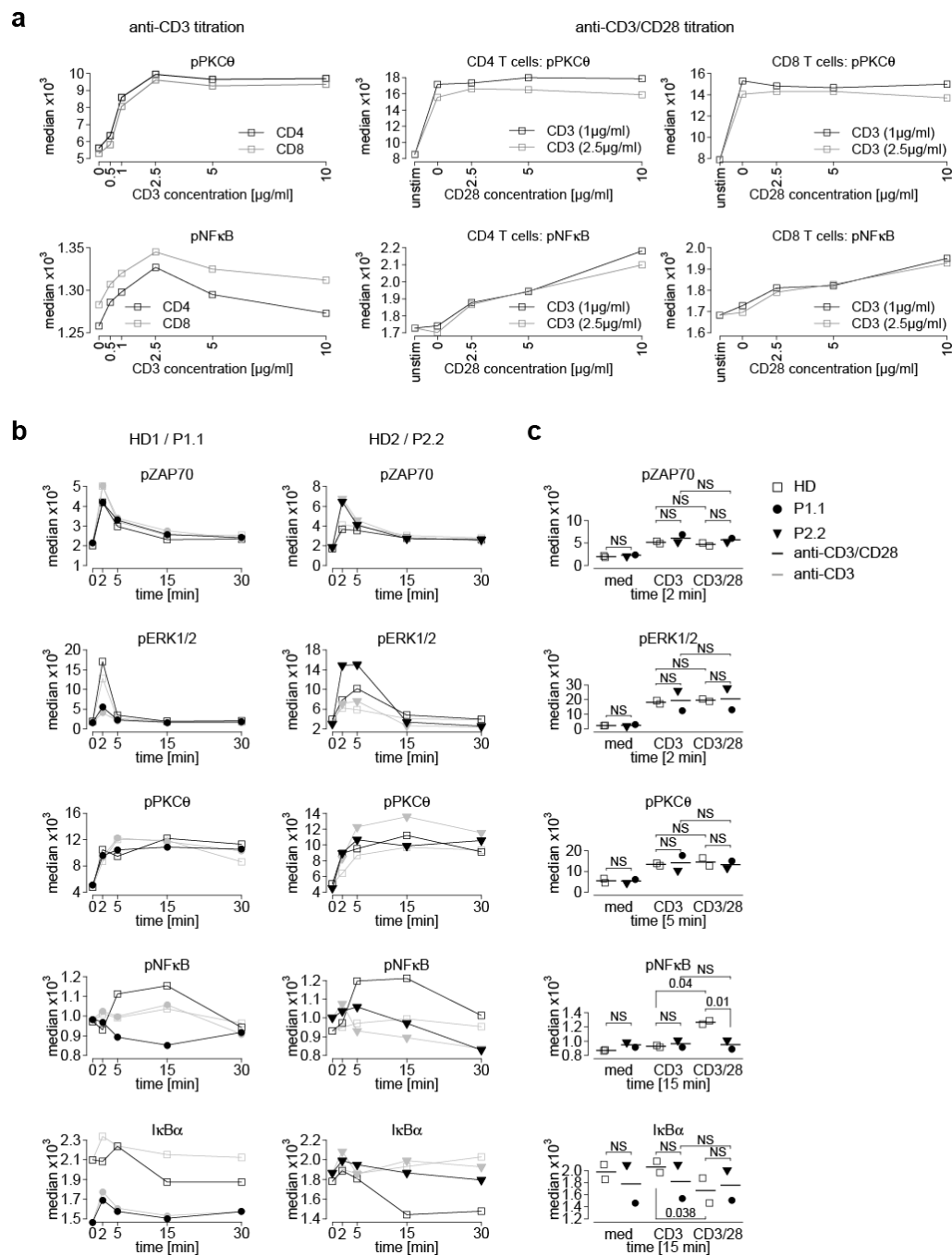
Supplementary Figure 3. *CARMIL2* c.871+1G>T leads to skipping of exon 11 and a premature stop codon. **(a)** Schemes of wildtype (HD) *CARMIL2* gDNA with exon-intron boundaries and cDNA with exon-exon boundaries and corresponding cDNA electropherogram. **(b)** Schemes of mutant c.871+1G>T (P2.1) *CARMIL2* gDNA with exon-intron boundaries and cDNA with exon-exon boundaries and corresponding cDNA electropherogram. The G>T transition is depicted in red, exonic bases in capital and intronic bases in small letters.



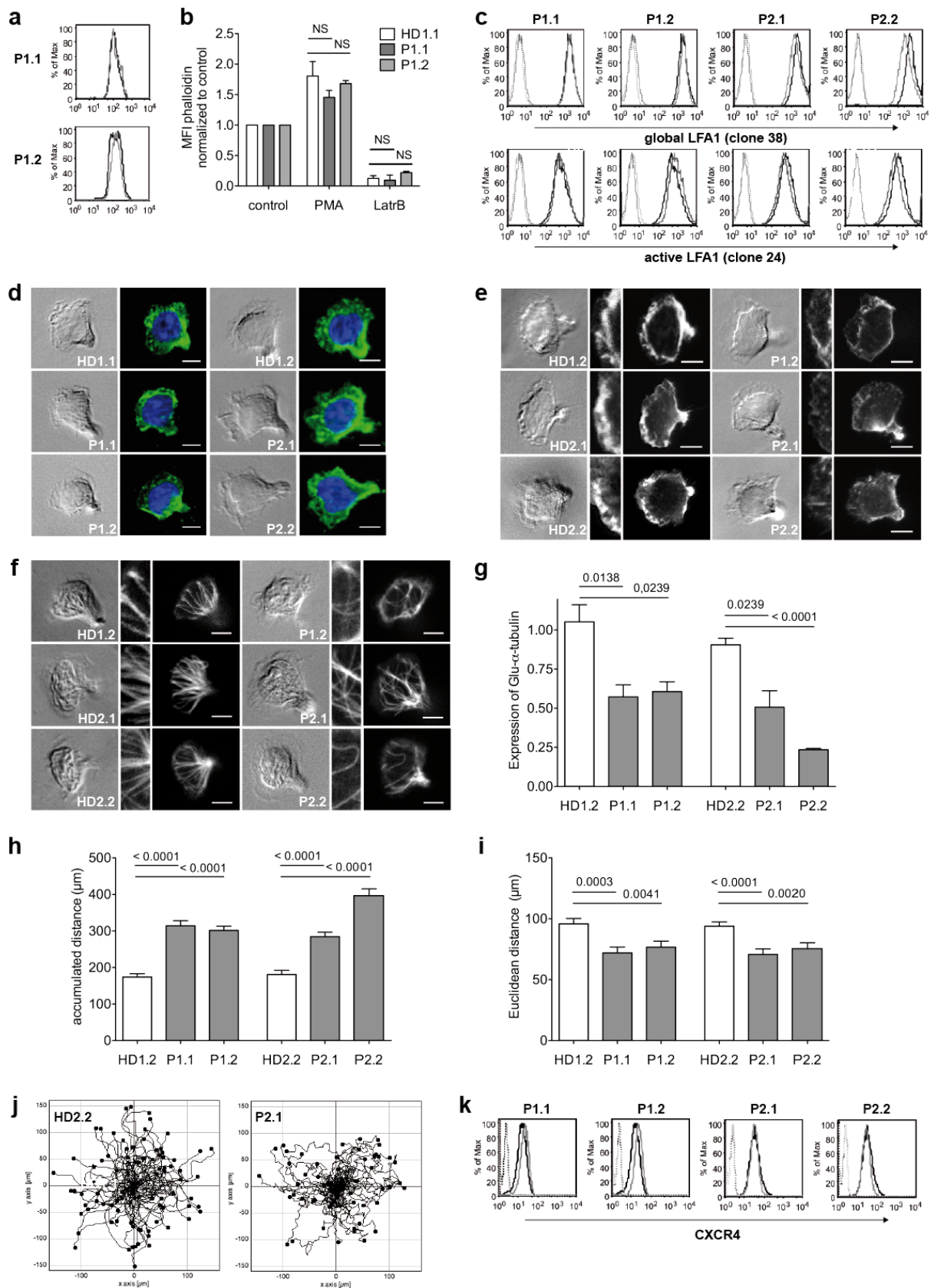
Supplementary Figure 4. CARMIL2-deficiency does not interfere with CD28 expression. **(a)** Representative histogram plot overlay of CD28 surface expression for four HD and four patients. **(b)** CFSE dilution and live cell rate determined by 7-AAD exclusion in CD4 and CD8 T cells stimulated for five days with decreasing anti-CD3 bead to cell ratios and PMA/ionomycin with increasing PMA concentrations.



Supplementary Figure 5. CARMIL2-deficient T cells have reduced CD28-dependent activation-induced cell death. Dot plots of 7-AAD enrichment and CFSE dilution in CD4 and CD8 T cells left unstimulated (medium), or stimulated for five days with anti-CD3, anti-CD3/CD28 or PMA/ionomycin (P/I) and summary of CD4 and CD8 T cell death percentages for five HD (open squares), P1.1 (black circle), P1.2 (black rhomb), P2.1 (black up-pointing triangle) and P2.2 (black down-pointing triangle). Small horizontal lines indicate the median. Each symbol represents an individual donor. Data are representative for two independent experiments with $n=2$. Significance levels are calculated with Welch's t -test and indicated in the summary graphs (NS = non significant).

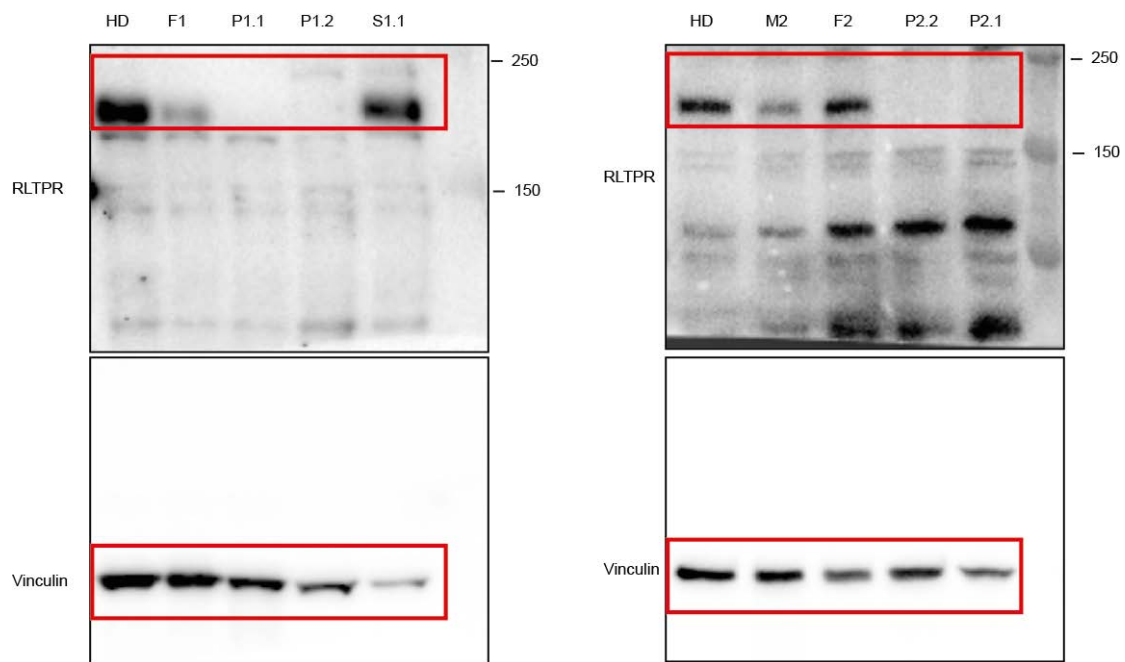


Supplementary Figure 6. CARMIL2-deficiency impairs CD28 co-signaling. **(a)** Stimulation titration curves with increasing anti-CD3 and anti-CD28 concentrations for pPKC θ and pNF- κ B (p65) in CD4 and CD8 T lymphoblasts from HD. **(b)** Median of pZAP70, pERK1/2, pPKC θ , pNF- κ B (p65) and I κ B α in CD8 T lymphoblasts from HD1 and HD2 (open squares), P1.1 (black circle) and P2.2 (black down-pointing triangle) stimulated with anti-CD3 and anti-CD3/CD28 for 0, 2, 5, 15 and 30 min by flow cytometry. **(c)** Summary of median (phospho-) protein levels for two HD and two patients at the indicated time points with $n=3$. Significance levels are calculated with Welch's t -test (NS = non significant).

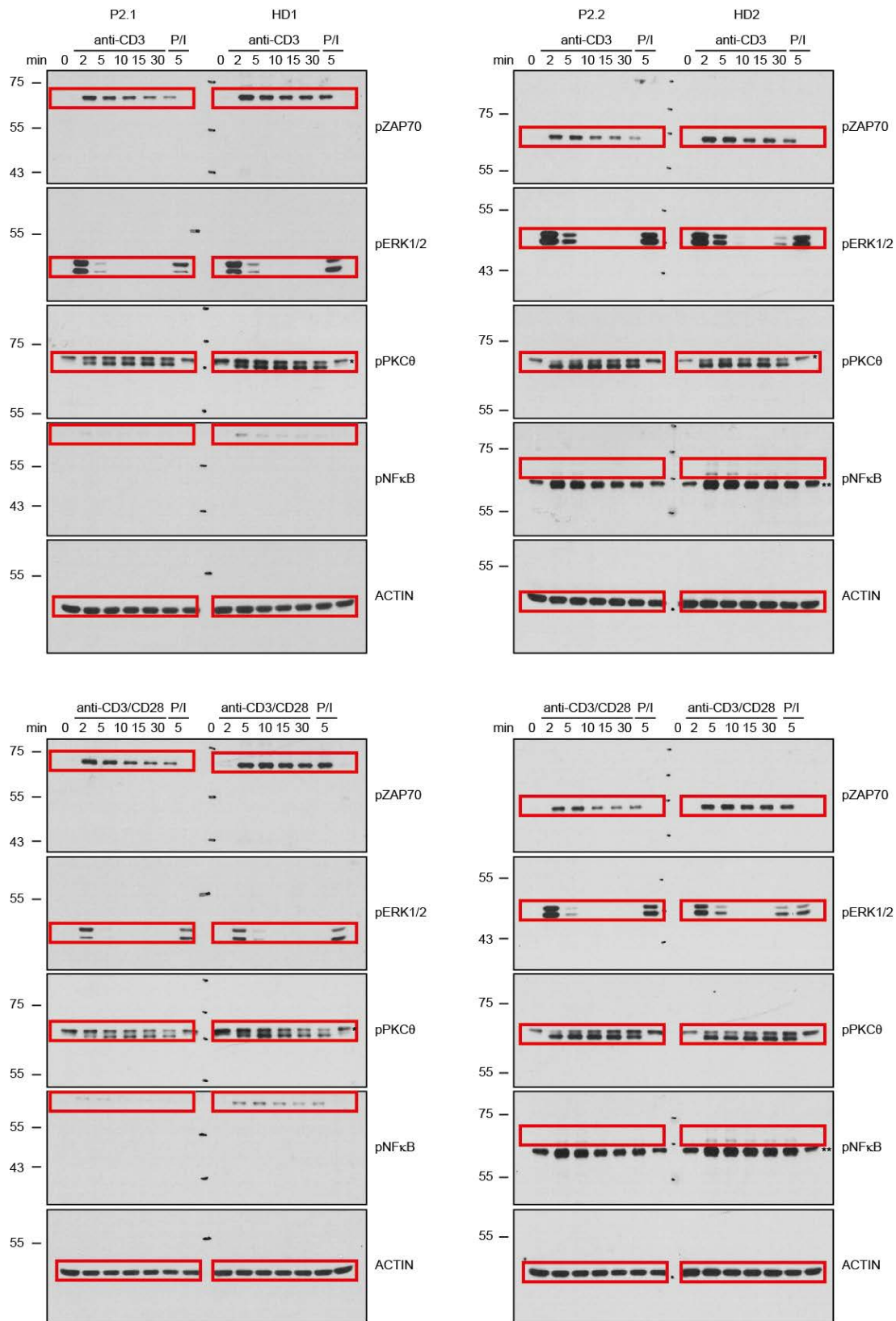


Supplementary Figure 7. CARMIL2-deficiency results in impaired cytoskeletal architecture and directness of migration. (a) F-actin amount detected by MFI of phalloidin-Alexa596

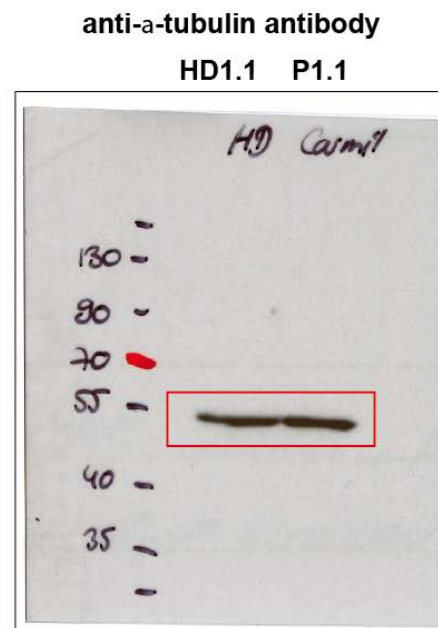
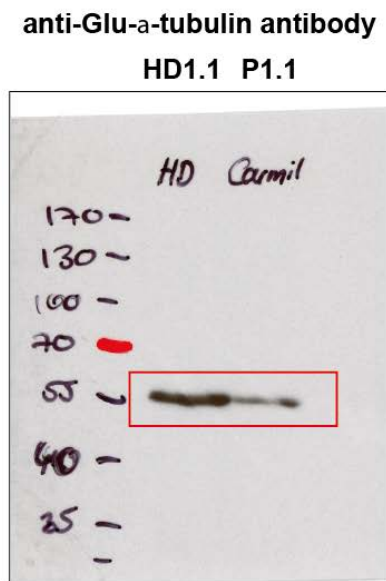
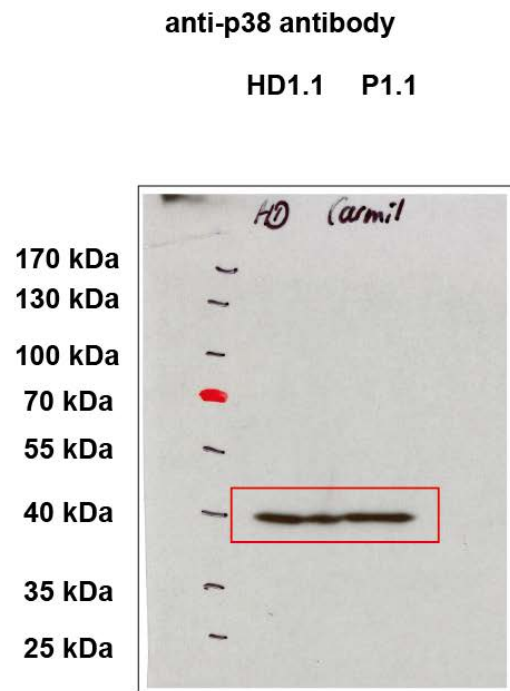
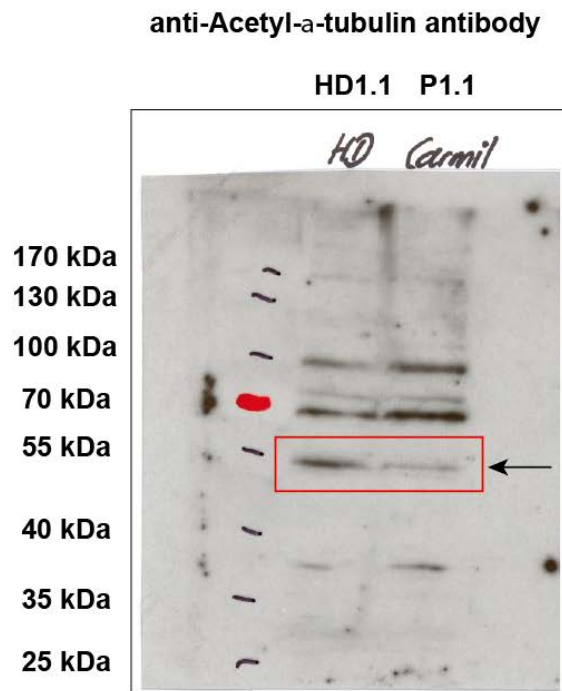
binding (black line, HD1.1; grey line, P1.1 or P1.2). **(b)** Quantification of F-actin in PMA or latrunculin B (LatrB) treated T lymphoblasts normalized to control cells of HD1.1, P1.1 and P1.2 (mean \pm s.e.m., n=2). **(c)** Comparable amount of global LFA1 (clone 38) or active LFA1 (clone 24) in HD1.1 or HD2.1 compared to P1.1 and P1.2 or P2.1 and P2.2 T lymphoblasts, respectively. One representative histogram of two independent experiments is shown (black line, HD; grey line, patients; dotted lines, respective mAb controls). **(d, e, f)** DIC and fluorescence images of LFA1 (**d**, green; DAPI blue), F-actin (**e**) and tubulin (**f**) in T lymphoblasts from HD and patients migrating on ICAM1 (scale bars 5 μ m). Fluorescence images in (**d**) are maximum intensity projections of acquired z-stacks. Fluorescence pictures in (**e, f**) are single images at the level of the adhesion plane. Details of fluorescence images are shown in the middle. **(g)** Quantification of stable α -tubulin on immunoblots (Fig. 6c) as detected by Glu- α -tubulin normalized to the amount of Glu- α -tubulin in T lymphoblasts from HD1.1 (mean \pm s.e.m., n \geq 3). **(h, i, j)** Spontaneous migration of HD and patient T lymphoblasts on ICAM1 in 2D and quantification of the accumulated distance (**h**, length of migration paths) and Euclidean distance (**i**, length of straight line between cell start and end point) (mean \pm s.e.m.). **(j)** Paths of cell migration from HD2.2 and P2.1 are visualized on trajectory plots (n=99). **(k)** Comparable surface expression of the CXCL12 receptor CXCR4 detected by flow cytometry in HD1.1 or HD2.1 compared to P1.1 and P1.2 or P2.1 and P2.2, respectively. One representative histogram out of two independent experiments (black line, HD; grey line, patient T cells, dotted lines, respective mAb controls). Significance levels are calculated with the two-sided unpaired Student's *t*-test and indicated in the summary graphs (NS = non significant).



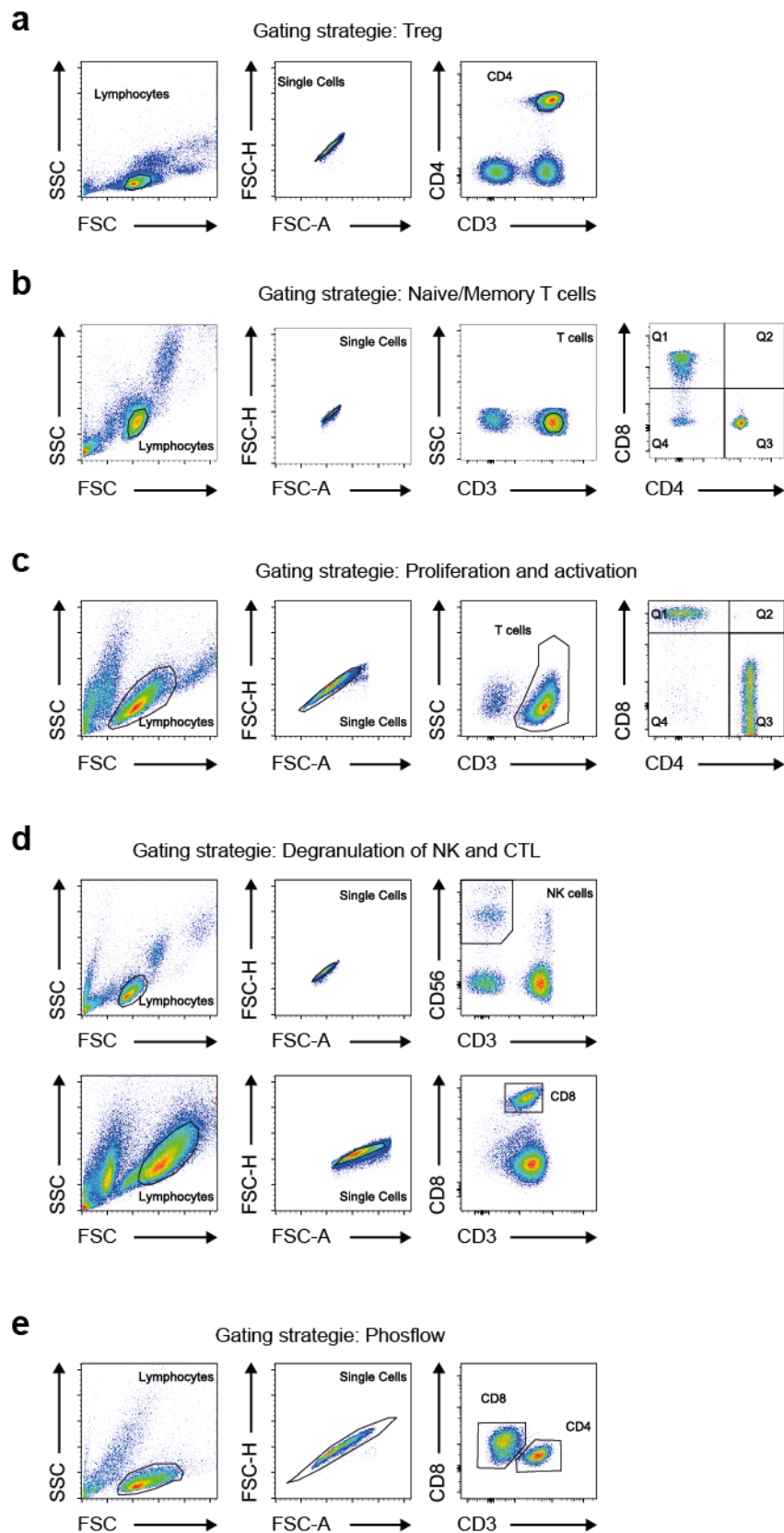
Supplementary Figure 8. Uncropped original immunoblots shown in Figure 2. The cropped areas are marked in red. Molecular weight markers are indicated in kDa.



Supplementary Figure 9. Uncropped original immunoblots shown in Figure 7. The cropped areas are marked in red. Molecular weight markers are indicated in kDa. * non-specific band. ** blots were reprobed with pZAP70 antibody.



Supplementary Figure 10. Uncropped original immunoblots shown in Figure 8c. The cropped areas are marked in red. Molecular weight markers are indicated in kDa.



Supplementary Figure 11. The gating strategies used in Fig. 3a (a), in Fig. 3b and Supplementary Fig. 4a (b), in Fig. 4a, 4b and 5a and Supplementary Fig. 5(c), in Fig. 6a-c (d) and in Fig. 7b and Supplementary Fig. 6 (e).

Supplementary Table 1. Histopathological and histochemical characterization of EBV⁺ SMT from P1.2.

Marker	Result
Morphology	Spindle cells with fusiform or ovoid nuclei
Smooth muscle actin	Positive
Calponin	Positive
Pan-cytokeratin	Negative
Desmin	Negative
CD34	Negative
C117	Negative
S100	Negative
Ki67	Positive in 15-20%
EBER	Positive
LMP1	Negative
LMP2A	Scattered positive
EBNA2	Partially positive
ZEBRA	Negative
CD21	Negative
P53	Partial expression, no overexpression
C-MYC	Partial expression, no gene rearrangement
CD80/CD86	Negative

Supplementary Tables 2. Family 1 immune phenotype.

2a. EBV, CMV genome and antibody counts.

Family 1			P1.1		P1.2	
Parameter*	Material	Method	Age 7y8m		Age 5y2m	
Epstein-Barr virus (EBV)	Serum	PCR [#]	negative		negative	
Epstein-Barr virus (EBV)	Colon	PCR	1,600 copies/ml		not done	
Epstein-Barr virus (EBV)	Stool	PCR	not done		350 copies/ml	
Epstein-Barr virus (EBV)	Urine	PCR	not done		900 copies/ml	
Cytomegalovirus (CMV)	Urine	PCR	not done		160,000 copies/ml	
EBV-VCA IgM	Serum	EIA [§]	21 AU/ml (positive)		negative	
EBV-VCA IgG	Serum	EIA	26 AU/ml (positive)		137 U/ml (positive) [¶]	
EBV-VCA IgA	Serum	IFT [†]	negative		not done	
EBV-EA IgG	Serum	EIA	negative		negative [¶]	
EBV-EA IgA	Serum	IFT	negative		not done	
EBV-EBNA IgG	Serum	EIA	negative		5 U/ml (positive) [¶]	
CMV IgM	Serum	EIA	not done		1:40	
CMV IgG	Serum	EIA	not done		4.8 AU/ml [¶]	

* Normal values are from the Max von Pettenkofer Institute, Ludwig-Maximilians-Universität, Munich, Germany; [#]PCR = polymerase chain reaction; [§]EIA = enzyme-linked immunosorbent assay; [¶]P1.2 has had immunoglobulin replacement therapy a few months before that; [†]IFT = indirect immunofluorescence test.

2b. T, B and NK cell counts.

Family 1				P1.1				P1.2			
		Normal value*		Age 7y2m		Age 7y3m		Age 5y2m		Age 5y6m	
Cell subset	Marker	#/μl	%	#/μl	%	#/μl	%	#/μl	%	#/μl	%
T cells	CD3 ⁺ per CD45 ⁺	700-4200	55-78	3430	77	3935	79	5530	72	2474	89
Helper T cells	CD3 ⁺ CD4 ⁺ per CD45 ⁺	300-2000	27-53	1960	44	2291	46	3380	44	1223	44
Cytotoxic T cells	CD3 ⁺ CD8 ⁺ per CD45 ⁺	300-1800	19-34	1069	24	1196	24	1834	24	1001	36
Activated T cells, B cells, monocytes	HLA-DR ⁺ per CD45 ⁺	250-2300	13-45	1425	32	1295	32	2534	33	639	23
Activated T cells	CD3 ⁺ HLA-DR ⁺ per CD45 ⁺	50-700	3-14	490	11	349	11	614	8	361	13
B cells	CD19 ⁺ per CD45 ⁺	200-1600	10-31	891	20	847	20	1843	24	222	8
NK cells	CD3 ⁻ CD16 ⁺ CD56 ⁺ per CD45 ⁺	90-900	4-26	134	3	150	3	154	2	56	2

* Normal values are from Comans-Bitter et al., J Pediatr 1997.

2c. B cell subset counts.

Family 1				P1.1		P1.2	
Cell subset	Marker	Normal value*		Age 7y2m		Age 5y2m	
		#/μl	%	#/μl	%	#/μl	%
B cells	CD19 ⁺ per lymphocyte gate	92-792	4.3-23.1	615	13.8	1244	16.2
Memory B cells	CD19 ⁺ CD27 ⁺	9-136	4.6-49.1	32	5.2	69	5.6
IgM memory B cells	CD19 ⁺ CD27 ⁺ IgM ⁺ IgD ⁺	1-43	0.2-12.3	25	4.0	51	4.1
Switched memory B cells	CD19 ⁺ CD27 ⁺ IgM ⁻ IgD ⁻	5-74	1.9-30.4	6	1.0	15	1.2
CD21 ^{low} CD38 ^{low} B cells	CD19 ⁺ CD21 ^{low} CD38 ^{low}	1-26	0.2-5.5	13	2.1	37	3

*Normal values are from Mayo Medical Laboratories, Test ID: IABCS.

2d. Immunoglobulin and specific antibody counts.

Family 1	P1.1*		P1.2*	
	Normal value [#]	Age 7y2m	Normal value	Age 5y2m
Total protein	6.0-8.0 g/l	8.0 g/l	6.0-8.0 g/l	6.8 g/dl
IgM	0.48-2.38 g/l	1.97 g/l	0.48-2.38 g/l	2.05 g/l
IgG	5.76-15.1 g/l	8.91 g/l	5.76-15.1 g/l	4.62 g/l [§]
IgG ₁	3.50-9.10 g/l	4.87 g/l	3.00-8.40 g/l	2.38 g/l [§]
IgG ₂	0.85-3.30 g/l	2.44 g/l	0.70-2.55 g/l	1.75 g/l [§]
IgG ₃	0.20-1.04 g/l	0.57 g/l	0.17-0.97 g/l	0.31 g/l [§]
IgG ₄	0.03-1.58 g/l	0.01 g/l	0.02-1.16 g/l	<0.01 g/l [§]
IgA	0.46-3.04 g/l	1.23 g/l	0.46-3.04 g/l	1.88 g/l
IgE	≤90 IU/ml	17.6 IU/ml	≤90 IU/ml	0.9 IU/ml
Tetanus toxoid IgG	≥0.1 IU/ml	0.09 IU/ml	≥0.1 IU/ml	0.15 IU/ml [§]
Diphtheria toxoid IgG	≥0.1 IU/ml	0.07 IU/ml	≥0.1 IU/ml	0.04 IU/ml [§]
Haemophilus influenzae typ b IgG	≥0.15 mg/l	<0.1 mg/l	≥0.15 mg/l	0.15 mg/l [§]
Pneumococcal polysaccharide IgG	≥21.6 mg/l	49.2 mg/l	≥21.6 mg/l	6.8 mg/l [§]

*P1.1 and P1.2 vaccination schedule: not documented, but reported to be in accordance with the vaccination schedule recommended in Yemen;

[#]Normal values are from and Baudner and Dati, J Lab Med 1996; Schauer et al., Clin Chem 2003; Schröder et al., Dtsch Med Wochenschr 1992; Efstratiou et al., Comm Dis Public Health 1999; Schauer et al., Clin Diagn Lab Immunol 2003;

[§]P1.2 has received immunoglobulin substitution several months before.

2e. T and B cell proliferation indices.

Family 1	P1.1*		P1.2*	
	Normal value [#]	Age 7y2m	Normal value	Age 5y2m
No stimulation	≥ 0.15	0.91	≥ 0.15	1.06
PHA [§] 1 µg/ml	≥ 0.15	1.48	≥ 0.15	0.46
PHA 0.1 µg/ml	≥ 0.15	1.46	≥ 0.15	0.07
OKT3 [†] 10 ng/ml	≥ 0.15	0.55	≥ 0.15	0.69
OKT3 1 ng/ml	≥ 0.15	0.25	≥ 0.15	0.41
SAC [¶] 0.001%	≥ 0.15	0.15	≥ 0.15	0.17
Antigen [°] 0.5/1.3 Lf/ml	≥ 0.15	0.03	≥ 0.15	0.02

* P2.1 vaccination schedule: not documented, but reported to be in accordance with the vaccination schedule recommended in Yemen;

[#]Normal values are in house derived;

[§]PHA = phytohemagglutinin;

[†]OKT3 = monoclonal anti-CD3ε antibody;

[¶]SAC = Staphylococcus aureus Cowan strain I;

[°]Antigen = tetanus and diphtheria toxoid.

Supplementary Tables 3. Family 2 immune phenotype.

3a. EBV, CMV, HHV6 genome and antibody counts.

Family 2			P2.1	P2.2
Parameter*	Material	Method	Age 14y1m	Age 11y10m
Epstein-Barr virus (EBV)	Serum	PCR [#]	330,000 copies/ml	negative
Cytomegalovirus (CMV)	Serum	PCR	70,000 copies/ml	negative
Human herpesvirus 6 (HHV6)	Serum	PCR	8,800 copies/ml	negative
EBV-VCA IgM	Serum	EIA [§]	13 AU/ml (positive)	negative
EBV-VCA IgG	Serum	EIA	>200 U/ml (positive)	143 U/ml (positive)
EBV-VCA IgA	Serum	IFT [†]	1:128 (positive)	1:64 (positive)
EBV-EA IgG	Serum	EIA	negative	negative
EBV-EA IgA	Serum	IFT	negative	negative
EBV-EBNA IgG	Serum	EIA	negative	negative
CMV IgM	Serum	EIA	positive	negative
CMV IgG	Serum	EIA	14 AU/ml (positive)	negative

*Normal values are from the Max von Pettenkofer Institute, Ludwig-Maximilians-Universität, Munich, Germany; [#]PCR = polymerase chain reaction; [§]EIA = enzyme-linked immunosorbent assay; [†]IFT = indirect immunofluorescence test.

3b. T, B and NK cell counts.

Family 2				P1.1		P1.2	
Cell subset	Marker	Normal value *		Age 13 y		Age 11 y	
		#/μl	%	#/μl	%	#/μl	%
T cells	CD3 ⁺ per CD45 ⁺	800-3500	52-78	3655	93	3377	86
Helper T cells	CD3 ⁺ CD4 ⁺ per CD45 ⁺	400-2100	25-48	1847	47	1964	50
Cytotoxic T cells	CD3 ⁺ CD8 ⁺ per CD45 ⁺	200-1200	9-35	1533	39	1178	30
Activated T cells, B cells, monocytes	HLA-DR ⁺ per CD45 ⁺	220-800	9-32	590	15	589	15
Activated T cells	CD3 ⁺ HLA-DR ⁺ per CD45 ⁺	20-200	1-8	393	10	118	3
B cells	CD19 ⁺ per CD45 ⁺	200-600	8-24	157	4	471	12
NK cells	CD3 ⁻ CD16 ⁺ CD56 ⁺ per CD45 ⁺	70-1200	6-27	39	1	79	2

*Normal values are from Comans-Bitter et al., J Pediatr 1997.

3c. B cell subset counts.

Family 2				P2.1		P2.2	
		Normal value *		Age 13y4m		Age 11y1m	
Cell subset	Marker	#/μl	%	#/μl	%	#/μl	%
B cells	CD19 ⁺ per lymphocyte gate	92-792	4.3-23.1	110	2.8	192	4.9
Memory B cells	CD19 ⁺ CD27 ⁺	9-136	4.6-49.1	14	12.4	10	5.4
IgM memory B cells	CD19 ⁺ CD27 ⁺ IgM ⁺ IgD ⁺	1-43	0.2-12.3	6	5.9	7	3.4
Switched memory B cells	CD19 ⁺ CD27 ⁺ IgM ⁻ IgD ⁻	5-74	1.9-30.4	6	5.9	3	1.5
CD21 ^{low} CD38 ^{low} B cells	CD19 ⁺ CD21 ^{low} CD38 ^{low}	1-26	0.2-5.5	6	5.4	4	2.3

* Normal values are from Mayo Medical Laboratories, Test ID: IABCS.

3d. Recent thymic emigrant cell counts.

Family 2				P2.1		P2.2	
		Normal value *		Age 13y4m		Age 11y1m	
Cell subset	Marker	#/μl	%	#/μl	%	#/μl	%
T cells	CD3 ⁺ per lymphocyte gate	800-3500	52-78	3270	83.2	3389	86.3
RTE cells	CD4 ⁺ CD31 ⁺ CD45RA ⁺ per CD3 ⁺	50-926	19.4-60.9	1001	62.1	1334	66.6

* Normal values are from Mayo Medical Laboratories, Test ID: 89504.

3e. CD45RA/CD45R0 T cell counts.

Family 2				P2.1		P2.2	
		Normal value *		Age 13y4m		Age 11y1m	
Cell subset	Marker	#/μl	%	#/μl	%	#/μl	%
T cells	CD3 ⁺ per lymphocyte gate	800-3500	52-78	3262	83	3377	86
Helper T cells	CD4 ⁺ per CD3 ⁺	400-2100	25-48	1611	41	2003	51
CD45RA helper T cells	CD4 ⁺ CD45RA ⁺ per CD4 ⁺	135-893	21-75	1402	87	1742	87
CD45R0 helper T cells	CD4 ⁺ CD45R0 ⁺ per CD4 ⁺	56-411	11-44	209	13	260	13

* Normal values are from Mayo Medical Laboratories, Test ID: TCP.

3f. Aβ/γδ T cell counts.

Family 2				P2.1		P2.2	
Cell subset	Marker	Normal value*		Age 13y4m		Age 11y1m	
		#/μl	%	#/μl	%	#/μl	%
T cells	CD3 ⁺ per lymphocyte gate	800-3500	52-78	3270	83.2	3389	86.3
Aβ DN [#] T cells	TCRαβ ⁺ CD4 ⁻ CD8 ⁻ per CD3 ⁺	<35	<2	23	0.71	20	0.58
Γδ DN T cells	TCRγδ ⁺ CD4 ⁻ CD8 ⁻ per CD3 ⁺	n.a. [†]	3-10	217	6.64	221	6.52
Γδ SP [§] T cells	TCRγδ ⁺ CD4 ⁻ CD8 ⁺ per CD3 ⁺	n.a.	n.a.	163	4.99	112	3.31

* Normal values are from Mayo Medical Laboratories, Test ID: 82449;

[#]DN = double negative;

[§]SP = single positive;

[†]n.a. = not available.

3g. Immunoglobulin and specific antibody counts/vaccination responses.

Family 2	P2.1*		P2.2 [#]	
	Normal value [§]	Age 13y4m	Normal value	Age 11y1m
Total protein	6.0-8.0 g/dl	6.3 g/dl	6.0-8.0 g/dl	7.5 g/dl
IgM	0.4-2.3 g/l	1.6 g/l	0.4-2.3 g/l	2.1 g/l
IgG	7.0-16.0 g/l	11.3 g/l	7.0-16.0 g/l	10.5 g/l
IgG ₁	3.7-9.1 g/l	4.75 g/l	3.7-9.3 g/l	6.32 g/l
IgG ₂	1.10-4.85 g/l	5.41 g/l	1.0-4.0 g/l	3.10 g/l
IgG ₃	0.24-1.16 g/l	0.67 g/l	0.22-1.09 g/l	0.37 g/l
IgG ₄	0.052-1.961 g/l	0.179 g/l	0.043-1.9 g/l	0.133 g/l
IgA	0.7-4.0 g/l	3.5 g/l	0.7-4.0 g/l	2.6 g/l
IgE	≤200 IU/ml	75IU/ml	≤200 IU/ml	758 IU/ml
Tetanus toxoid IgG	≥0.1 IU/ml	0.02 IU/ml	≥0.1 IU/ml	<0.01 IU/ml
Diphtheria toxoid IgG	≥0.1 IU/ml	<0.01 IU/ml	≥0.1 IU/ml	<0.01 IU/ml
Haemophilus influenzae typ b IgG	≥0.15 mg/l	0.16mg/l	≥0.15 mg/l	0.78mg/l
Pneumococcal polysaccharide IgG	≥21.6 mg/l	38.1mg/l	≥21.6 mg/l	19.7 mg/l
Bacille Calmette-Guérin	scar	no scar	scar	no scar

* P2.1 vaccination schedule: 1x BCG, 4x oPV, 4x DPT, 4x Hib, 4x HB, 2x MMR, 1x YF 1x, 2x IN;

[#]P2.2 vaccination schedule: 1x BCG, 4x oPV, 4x DPT, 4x Hib, 4x HB, 1x MMR, 1x YF 1x, 2x IN;

[§]Normal values are from and Baudner and Dati, J Lab Med 1996; Schauer et al., Clin Chem 2003; Schröder et al., Dtsch Med Wochenschr 1992; Efstratiou et al., Comm Dis Public Health 1999; Schauer et al., Clin Diagn Lab Immunol 2003;

Supplementary Table 4. WES candidate variants for family 1 after filtering.

Position	Orig Var	RSID	EnsGene	HGNC ID	EnsTrans	Type	Variation	PolyPhen	SIFT	ROH*
chr16:67680638-67680638	A->AG	none	ENSG00000159753	CARMIL2	ENST00000334583	frameshift	489+G,*@167	n.a.	n.a.	yes
chr16:72992196-72992196	C->T	111320371	ENSG00000140836	ZFXH3	ENST00000268489	missense	1849G>A,617V>I	0.105	n.a.	yes
chr16:78458922-78458922	G->A	none	ENSG00000186153	WWOX	ENST00000566780	missense	761G>A,254R>H	1	0	yes
chr20:39792419-39792419	C->T	150381500	ENSG00000124181	PLCG1	ENST00000373271	missense	956C>T,319P>L	0.029	n.a.	no
chr16:72057118-72057118	C->T	none	ENSG00000102967	DHODH	ENST00000219240	missense	874C>T,292L>F	0.992	0	yes
chr16:82131973-82131973	C->A	none	ENSG00000086696	HSD17B2	ENST00000199936	missense	1096C>A,366H>N	0	0.37	yes

*ROH = candidate identified by WES located inside the regions identified by homozygosity mapping.

Supplementary Table 5. Primers used for Sanger sequencing.

Gene	Type of DNA	Mutation	Direction	Primer
<i>CARMIL2</i>	gDNA	c.489insG	Forward	5' GCCCCAAACTGAACAGAGCCATT 3'
<i>CARMIL2</i>	gDNA	c.489insG	Reverse	5' TCCTGGGTGAGAAGAAGATGCTTA 3'
<i>CARMIL2</i>	gDNA	c.871+1G>T	Forward	5' AGAGGAGAGTCTGGAGGCTTG 3'
<i>CARMIL2</i>	gDNA	c.871+1G>T	Reverse	5' CACTCAGCAGTTGGACAGACC 3'
<i>CARMIL2</i>	cDNA	c.871+1G>T	Forward	5' CCTTGAGGTCTCAGAACAGATTCTGC 3'
<i>CARMIL2</i>	cDNA	c.871+1G>T	Reverse	5' CTGCGAGATTCAGGAACGACAGTA 3'