Evaluation of frequency of CMV replication and disease complications reveals new cellular defects and a time dependent pattern in CVID patients

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Supplementary materials

Antibody panel composition

Anti-CD16 FITC, mouse IgG1. clone NKP15, BD Biosciences.

Anti-CD3 PerCP Cy5.5, mouse IgG1 k, clone SK7, BD Biosciences.

Anti-TCRγδ PE, mouse IgG1 k, clone B1, Biolegend.

Anti-CD69 PE-Cy7, mouse IgG1 k, clone FN50, BD Biosciences.

Anti-DNAM-1 (CD226) APC, mouse IgG1 k, clone 11A8, Biolegend.

Anti-CD38 AF700, mouse IgG1, clone LS198, Beckman Coulter.

Anti-CD8 APC-Cy7, mouse IgG1 k, clone SK1, Biolegend.

Anti-HLA-DR PB, mouse IgG2a k, clone L243, Biolegend.

Anti-CD45 KO, mouse IgG1, clone J33, Beckman Coulter.

Anti-CD19 BV605, mouse IgG1 k, clone SJ25C1, BD Biosciences.

Anti-CD56 BV650, mouse IgG1 k, clone 5.1H11, Biolegend.

Anti-CD4 BV786, mouse IgG2b k, clone OKT4, Biolegend.

Supplementary tables

Table S1. CVID V.S. non-CVID hID PATIENTS: IMMUNOLOGICAL VARIABLES

	TOTAL (52)	CVID (31)	NON-CVID (21)	MD	P value
IMMUNOGLOBULINS					
IgG (onset) (g/L)	4.3 (3.5-5.1)	3.1 (2.3-4.0)	6.0 (4.6-7.4)	-2.88	**0.0003**
IgA (g/L)	0.55 (0.36-0.75)	0.48 (-0.02-0.18)	1.0 (0.6-1.4)	-0.53	**0.0002**
IgM (g/L)	0.42 (0.29-0.56)	0.38 (0.18-0.59)	0.48 (0.33-0.64)	-0.10	**0.0294**
IgE (kU/L)	19.0 (8.2-29.9)	10.1 (2.7-17.5)	39.1 (7.9-70.4)	-29	**0.0175**
GENERAL IMMUNOPHENOTYPE (ABSOLUTE COUNT: CELLS/µL)					
Lymphocytes	2045 (1765-2325)	2118 (1698-2538)	1933 (1597-2268)	185	0.782
Lymphocytes (% of WBC)	34.0 (31.1-36.9)	35.3 (31.2-39.5)	31.8 (28.1-35.6)	3.5	0.208
Monocytes	383 (333-434)	369 (306-432)	404 (315-493)	-35	0.554
Monocytes (% of WBC)	6.5 (5.8-7.1)	6.3 (5.3-7.2)	6.8 (5.9-7.7)	-0.5	0.169
T-cells	1357 (1167-1547)	1446 (1177-1716)	1225 (956-1494)	221	0.097
T-cells (% of Lymphocytes))	67.0 (63.8-70.3)	69.3 (65.4-73.2)	63.5 (57.7-69.4)	5.7	0.141
B cells	248 (170-326)	266 (155-378)	220 (108-332)	46	0.961
B cells (% of Lymphocytes)	11.1 (8.6-13.5)	10.9 (7.9-13.8)	11.4 (6.8-16.0)	-0.56	0.811
NK-cells	182 (144-221)	172 (121-222)	198 (135-261)	-26	0.175
NK-cells (% of Lymphocytes)	9.2 (7.5-10.8)	8.6 (6.5-10.7)	10.0 (7.0-10.7)	-1.4	0.364
NKT	97 (46-149)	58 (31-85)	156 (32-279)	-98	**0.027**
NKT-cells (% of Lymphocytes)	4.3 (2.2-6.5)	2.7 (1.8-3.6)	6.8 (1.5-12.1)	-4.1	0.080
Lineage negative (Lin-)	163 (137-188)	173 (134-211)	148 (118-179)	24	0.529
Lin- cells (% of lymphocytes)	8.8 (7.3-10.2)	9.4 (7.3-11.5)	7.8 (5.8-9.8)	1.6	0.459
B CELLS IMMUNOPHENOTYPE (% OF TOTAL B CELLS)					
Naïve $IgM^+IgD^{++}CD38^+CD27^-CD21^+$	50.4 (43.1-57.8)	54.4 (46.3-62.6)	39.2 (22.4-56.1)	15.2	0.0703
CD21low	8.9 (5.8-12.1)	9.4 (5.3-13.5)	7.7 (3.0-12.4)	1.7	0.888

IgM$^+$IgD$^+$CD38^{low}CD27$^-$CD21^{low}					
Class-switched memory	5.3 (3.3-7.4)	4.1 (1.6-6.6)	8.4 (4.9-11.9)	-4.3	**0.0130**
IgM$^-$IgD$^-$CD38$^+$CD27$^+$CD21$^+$					
Non-switched memory	12.7 (7.5-17.8)	8.3 (4.1-12.5)	25.1 (9.9-40.2)	-16.8	**0.0087**
IgM^{++}IgD$^+$CD38$^+$CD27$^+$CD21$^+$					
Transitional	6.6 (3.2-9.9)	7.6 (3.2-12.0)	3.7 (-0.1-7.5)	3.9	0.104
IgM^{++}IgD^{++}CD38^{++}CD27$^-$CD21$^+$					
Plasmablasts	0.34 (0.09-0.60)	0.37 (0.05-0.69)	0.27 (-0.18-0.73)	0.10	0.962
IgM$^{-/+}$IgD$^-$CD38^{+++}CD27^{++}CD21$^+$					
T-CELLS IMMUNOPHENOTYPE					
αβ T-cells	1327 (1140-1515)	1409 (1145-1673)	1206 (935-1477)	203	0.113
αβ T-cells (% of T-cells)	97.7 (97.1-98.2)	97.4 (96.8-98.1)	98.0 (97.0-99.1)	-0.6	**0.020**
γδ T-cells	29.8 (21.7-37.9)	37.1 (24.8-49.4)	19.0 (11.4-26.5)	18.1	**0.004**
γδ T-cells (% of T-cells)	2.3 (1.8-2.8)	2.6 (1.9-3.2)	1.9 (0.9-3.0)	0.6	**0.019**
αβ CD4+ T	808 (697-918)	805 (667-942)	812 (614-1010)	-8	0.671
αβ CD4+ T (% of αβ T-cells)	61.9 (58.8-65.1)	58.7 (54.4-63.2)	66.6 (62.8-70.3)	-7.8	**0.012**
αβ CD8+ T	455 (360-550)	528 (384-672)	341 (258-425)	187	**0.045**
αβ CD8+ T (% of αβ T-cells)	33.0 (30.1-35.9)	35.7 (31.6-39.7)	28.8 (25.2-32.4)	6.9	**0.016**
αβ DN T-cells	59.3 (46.1-72.6)	68.0 (48.5-87.4)	46.0 (30.6-61.4)	22.0	0.095
αβ DN T-cells (% of αβ T-cells)	4.6 (3.8-5.4)	5.0 (3.9-6.1)	4.0 (2.7-5.3)	1.0	0.163
αβ CD4+CD8+ T	9.3 (4.9-13.6)	8.5 (2.6-14.3)	10.5 (3.5-17.6)	-2.0	0.931
αβ CD4+CD8+ T (% of αβ T-cells)	0.67 (0.40-0.94)	0.52 (0.24-0.80)	0.9 (0.3-1.5)	-0.38	0.871
NK IMMUNOPHENOTYPE (% OF TOTAL NK-CELLS)					
NK CD56^{dim}	168.0 (131.0-205.0)	157.3 (108.4-206.2)	168.4 (112.4-224.5)	-26.4	0.169
NK CD56^{dim} %	90.8 (87.9-93.6)	90.6 (86.4-94.8)	91.0 (87.0-95.1)	-0.45	0.345
NK CD56^{bright}	11.4 (9.1-13.7)	10.3 (7.8-12.8)	13.1 (8.5-17.6)	-2.8	0.335
NK CD56^{bright} %	7.7 (6.3-9.0)	7.31 (6.11-8.51)	8.2 (5.2-11.2)	-0.86	0.505

Quantitative variables are expressed as means with a 95% confidence interval, while qualitative variables are represented as absolute frequencies with percentages relative to the total of the respective column. P values were calculated by either unpaired two-tailed Student's t-test or Mann-Whitney u test according to variable distribution and sample size. OR: odds ratio; MD: mean difference; DN: double negative

Table S2. Comparison between CVID patients with active CMV replication vs non-replicating

	Total (31)	CMV (5)	Non/CMV (26)	OR/ MD	P value (univar.)
SAMPLE DEMOGRAPHICS					
Male	14(45%)	1(20%)	13(50%)	0.25	0.3445
Female	17(55%)	4(80%)	13(50%)	4.0	0.3445
Age	50.4 (44.1-56.7)	56 (37.0-75.0)	49.4 (42.3-56.4)	6.7	0.4352
CLINICAL VARIABLES					
Age at diagnosis	39.0 (32.3-45.8)	41.8 (18.8-64.8)	38.5 (30.9-46.1)	3.3	0.6861
Disease duration	13.7 (8.8-18.5)	16.2 (3.6-28.8)	13.2 (7.6-18.7)	3.0	0.4078
Ig replacement therapy (IGRT)	23(74%)	4(80%)	19(73%)	1.474	>0.9999
IGRT duration	8.1 (4.8-11.4)	12.0 (1.7-22.3)	7.2 (3.6-10.8)	4.8	0.3112
Infections	29(94%)	5(100%)	24(92%)	Infinity	>0.9999
Autoimmunity	19(61%)	3(60%)	16(62%)	0.9375	>0.9999
Splenomegaly	12(39%)	5(100%)	7(27%)	Infinity	**0.0047**
Granulomatosis	6(19%)	2(40%)	4(15%)	3.667	0.2020
Malignancies	6(19%)	1(20%)	5(19%)	1.05	0.9682
Lymphadenomegaly	12(39%)	4(80%)	8(31%)	9.0	0.0600
Lung involvement	13(42%)	4(80%)	9(35%)	7.556	0.1337
Atopy	10(32%)	0(0%)	10(38%)	0	0.1472
Blood EBV replication	6(19%)	3(60%)	3(12%)	11.5	**0.0376**
IMMUNOGLOBULINS					
IgG (onset) (g/L)	3.1 (2.3-4.0)	1.6 (-1.1-4.4)	3.3 (2.4-4.2)	-1.7	0.2740
IgA (g/L)	0.48 (-0.02-0.18)	0.11 (-0.16-0.38)	0.56 (-0.04-1.15)	-0.45	0.2498
IgM (g/L)	0.38 (0.18-0.59)	0.35 (-0.25-0.95)	0.39 (0.15-0.62)	-0.04	0.8870
IgE (kU/L)	10.1 (2.7-17.5)	2.2 (-4.0-8.5)	11.9 (2.9-20.9)	-9.7	0.3323
GENERAL IMMUNOPHENOTYPE (ABSOLUTE COUNT: CELLS/μL)					
Lymphocytes	2118 (1698-2538)	2220 (157-4283)	2098 (1669-2528)	121	0.584
Lymphocytes (% of WBC)	35.3 (31.2-39.5)	38.1 (17.9-58.2)	34.9 (30.6-39.1)	3.2	0.480
Monocytes	369 (306-432)	376 (55-698)	368 (305-431)	9	0.696
Monocytes (% of WBC)	6.3 (5.3-7.2)	6.0 (4.4-7.5)	6.3 (5.1-7.5)	-0.4	1.000
T cells	1446 (1177-1716)	1675 (226-3124)	1402 (1141-1664)	273	0.897
T cells (% of Lymphocytes)	69.3 (65.4-73.2)	77.3 (70.6-84.1)	67.7 (63.4-72.1)	9.6	**0.041**
B cells	266 (155-378)	252 (-177-681)	261 (142-380)	-9	0.514
B cells (% of Lymphocytes)	10.9 (7.9-13.8)	8.3 (1.6-14.9)	11.4 (8.0-14.7)	-3.1	0.548
NK cells	172 (121-222)	97 (23-170)	186 (127-245)	-90	0.235
NK cells (% of Lymphocytes)	8.6 (6.5-10.7)	5.2 (1.3-9.1)	9.3 (6.9-11.6)	-4.0	0.159
NKT-LIKE	58 (31-85)	87 (-74-249)	52 (28-76)	35	0.735
NKT-LIKE cells (% of Lymphocytes)	2.7 (1.8-3.6)	2.7 (-0.6-6.1)	2.7 (1.7-3.7)	0.06	0.856
Lineage negative (Lin-)	173 (134-211)	129 (36-221)	181 (137-225)	-52	0.358
Lin- cells (% of lymphocytes)	9.4 (7.3-11.5)	7.8 (1.8-13.8)	9.7 (7.4-12.1)	-1.9	0.658

B CELLS IMMUNOPHENOTYPE (% OF TOTAL B CELLS)

Naïve	54.4	58.5	53.7	4.8	0.8987
IgM$^+$IgD^{++}CD38$^+$CD27$^-$CD21$^+$	(46.3-62.6)	(39.3-77.7)	(44.1-63.2)		
CD21low	9.4	15.4	8.2	7.2	0.1724
IgM$^+$IgD$^+$CD38^{low}CD27$^-$CD21^{low}	(5.3-13.5)	(-5.0-35.7)	(4.2-12.3)		
Class-switched memory	4.1	2.3	4.5	-2.2	0.9688
IgM$^-$IgD$^-$CD38$^+$CD27$^+$CD21$^+$	(1.6-6.6)	(-0.1-4.8)	(1.5-7.4)		
Non-switched memory	8.3	3.6	9.1	-5.5	0.8450
IgM^{++}IgD$^+$CD38$^+$CD27$^+$CD21$^+$	(4.1-12.5)	(1.7-5.4)	(4.2-14.1)		
Transitional	7.6	8.2	7.5	0.7	0.2448
IgM^{++}IgD^{++}CD38^{++}CD27$^-$CD21$^+$	(3.2-12.0)	(0.04-16.4)	(2.2-12.7)		
Plasmablasts	0.37	0.78	0.29	0.49	0.5366
IgM$^{-/+}$IgD$^-$CD38^{+++}CD27^{++}CD21$^+$	(0.05-0.69)	(-1.18-2.74)	(0.01-0.56)		

T CELLS IMMUNOPHENOTYPE

αβ T cells	1409	1644	1364	280	0.938
	(1145-1673)	(197-3092)	(1112-1616)		
αβ T cells	97.4	97.9	97.4	0.6	0.176
(% of T cells)	(96.8-98.1)	(95.4-100.4)	(96.7-98.0)		
γδ T cells	37.1	30.5	38.4	-7.9	0.480
	(24.8-49.4)	(-8.2-69.2)	(24.5-52.3)		
γδ T cells	2.6	2.1	2.6	-0.6	0.176
(% of T cells)	(1.9-3.2)	(-0.5-4.6)	(2.0-3.3)		
αβ CD4+ T	805	770	811	-42	0.775
	(667-942)	(306-1233)	(657-966)		
αβ CD4+ T	58.7	50.8	60.3	-9.5	0.195
(% of αβ T cells)	(54.4-63.2)	(34.4-67.2)	(55.7-65.0)		
αβ CD8+ T	528	787	478	309	0.417
	(384-672)	(-139-1713)	(364-593)		
αβ CD8+ T	35.7	44.0	34.1	9.9	0.081
(% of αβ T cells)	(31.6-39.7)	(31.0-56.9)	(29.8-38.3)		
αβ DN T cells	68.0	68.3	67.9	0.5	0.775
	(48.5-87.4)	(-6.8-143.4)	(46.6-89.2)		
αβ DN T cells	5.0	4.5	5.1	-0.6	0.257
(% of αβ T cells)	(3.9-6.1)	(-0.5-9.6)	(4.0-6.2)		
αβ CD4+CD8+ T	8.5	19.5	6.4	13.1	0.979
	(2.6-14.3)	(-25.0-64.1)	(3.0-9.8)		
αβ CD4+CD8+ T	0.52	0.70	0.49	0.21	0.735
(% of αβ T cells)	(0.24-0.80)	(-0.40-1.80)	(0.18-0.79)		
αβ CD4+DR+ T	36.1	35.3	36.2	-0.9	0.815
	(27.6-44.5)	(4.1-66.5)	(26.9-45.6)		
αβ CD4+DR+ T	5.1	5.6	5.0	0.6	0.815
(% of CD4 αβ T cells)	(3.9-6.2)	(0.7-10.5)	(3.8-6.2)		
αβ CD4+CD69+ T	11.6	11.2	11.7	-0.5	0.938
	(8.2-15.1)	(1.4-21.0)	(7.7-15.7)		
αβ CD4+CD69+ T	1.6	1.5	1.6	-0.02	0.696
(% of CD4 αβ T cells)	(1.0-2.1)	(0.3-2.8)	(0.9-2.2)		
αβ CD4+DR+CD69+ T	1.1	1.6	1.0	0.6	0.938
	(0.6-1.6)	(-1.3-4.6)	(0.6-1.4)		
αβ CD4+DR+CD69+ T	0.2	0.2	0.1	0.1	0.658
% of CD4 αβ T cells	(0.1-0.2	(-0.2-0.6)	(0.07-0.2)		
αβ CD4+DR+CD38+ T	13.8	23.7	11.9	11.8	0.063
	(8.9-18.8)	(2.5-45.0)	(7.0-16.9)		
αβ CD4+DR+CD38+ T	2.1	3.7	1.7	2.0	0.103
(% of CD4 αβ T cells)	(1.4-2.8)	(0.6-6.8)	(1.1-2.4)		
αβ CD4+CD38+CD69+ T	4.6	4.0	4.7	-0.7	0.620
	(3.0-6.3)	(1.8-6.2)	(2.8-6.7)		
αβ CD4+CD38+CD69+ T	0.6	0.6	0.6	-0.01	0.897
(% of CD4 αβ T cells)	(0.4-0.8)	(0.2-1.0)	(0.4-0.8)		
αβ CD8+DR+ T	32.2	40.1	30.7	9.5	0.214
	(22.1-42.3)	(15.8-64.4)	(19.0-42.3)		
αβ CD8+DR+ T	6.9	7.8	6.7	1.1	0.735
(% of CD8 αβ T cells)	(5.3-8.4)	(0.9-14.7)	(5.1-8.3)		
αβ CD8+CD69+ T	22.1	28.6	20.9	7.7	0.235
	(6.7-37.6)	(-8.7-65.9)	(2.9-38.8)		
αβ CD8+CD69+ T	4.3	3.4	4.4	-1.0	0.115
(% of CD8 αβ T cells)	(1.3-7.3)	(2.9-3.9)	(0.8-8.1)		
αβ CD8+DR+CD69+ T	1.6	2.6	1.4	1.2	0.214

	(1.1-2.1)	(-0.3-5.5)	(1.0-1.9)		
αβ CD8+DR+CD69+ T	0.4	0.5	0.3	0.1	0.448
(% of CD8 αβ T cells)	(0.3-0.5)	(0.03-0.9)	(0.2-0.5)		
αβ CD8+DR+CD38+ T	13.5	21.3	12.0	9.3	0.055
	(8.2-18.8)	(4.8-37.9)	(6.1-17.9)		
αβ CD8+DR+CD38+ T	2.7	4.0	2.4	1.6	0.214
(% of CD8 αβ T cells)	(1.9-3.4)	(0.3-7.7)	(1.7-3.1)		
αβ CD8+CD38+CD69+ T	3.8	9.4	2.7	6.7	0.103
	(1.5-6.1)	(-7.0-25.8)	(1.4-4.0)		
αβ CD8+CD38+CD69+	0.7	0.9	0.6	0.3	0.115
(% of CD8 αβ T cells)	(0.4-0.9)	(0.3-1.5)	(0.3-0.9)		

NK IMMUNOPHENOTYPE (% OF TOTAL NK CELLS)

NK CD56^{dim}	157.3	66.3	174.8	-108.6	0.071
	(108.4-206.2)	(34.7-97.9)	(118.8-230.9)		
NK CD56^{dim} %	90.6	80.3	92.6	-12.2	0.280
	(86.4-94.8)	(46.3-114.3)	(91.2-93.9)		
NK CD56^{bright}	10.3	5.6	11.2	-5.5	0.103
	(7.8-12.8)	(3.4-7.8)	(8.3-14.1)		
NK CD56^{bright} %	7.31	6.84	7.39	-0.59	0.979
	(6.11-8.51)	(4.16-9.51)	(6.03-8.76)		
NK DR+	16.7	7.0	18.5	-11.6	**0.048**
	(11.8-21.5)	(4.3-9.7)	(13.0-24.1)		
NK DR+ %	13.2	9.3	13.9	-4.6	0.735
	(8.8-17.6)	(3.6-15.1)	(8.7-19.2)		
NK CD69+	9.5	3.3	10.7	-7.3	0.387
	(4.8-14.1)	(1.2-5.4)	(5.2-16.2)		
NK CD69+ %	6.7	4.2	7.2	-3.0	0.735
	(3.4-10.0)	(0.6-7.9)	(3.3-11.1)		
NK DR+CD69+	2.7	0.5	3.1	-2.6	0.448
	(-0.2-5.5)	(-0.03-1.0)	(-0.3-6.5)		
NK DR+CD69+ %	2.8	0.5	3.2	-2.7	0.696
	(-0.3-5.8)	(0.2-0.9)	(-0.4-6.9)		

PUTATIVE LYMPHOID PRECURSORS

PUTATIVE CD56-CD16+	11.3	5.94	12.34	-6.40	0.129
PRECURSORS	(7.5-15.1)	(-3.16-15.05)	(8.04-16.64)		
PUTATIVE CD56-CD16+	3.45	3.61	3.42	0.19	0.514
PRECURSORS%	(2.23-4.67)	(-2.98-10.20)	(2.23-4.61)		
LIN-DNAM^{bright}	9.99	3.74	11.19	-7.45	0.195
	(6.56-13.41)	(-0.46-7.93)	(7.28-15.09)		
LIN-DNAM^{bright} %	3.06	1.60	3.34	-1.75	0.514
	(1.85-4.27)	(0.41-2.78)	(1.92-4.77)		

Quantitative variables were expressed as means with a 95% confidence interval, while qualitative variables were represented as absolute frequencies with percentages relative to the total of the respective column. P values were calculated by either unpaired two-tailed Student's t-test or Mann-Whitney u test according to variable distribution and sample size. OR: odds ratio; MD: mean difference; DN: double negative; Univar.: univariate analysis.

Table S3. Comparison between CVID patients with active EBV replication vs non-replicating

	Total (31)	EBV (6)	Non-EBV (25)	OR/ MD	P value (univar.)
SAMPLE DEMOGRAPHICS					
Male	14(45%)	3(50%)	11(44%)	1.273	>0.9999
Female	17(55%)	3(50%)	14(56%)	0.7857	>0.9999
Age	50.4 (44.1-56.7)	49.8 (30.0-69.7)	50.6 (43.5-57.6)	-0.7	0.9274
CLINICAL VARIABLES					
Age at diagnosis	39.0 (32.3-45.8)	37.5 (16.2-58.8)	39.4 (31.8-47.0)	-1.9	0.9901
Disease duration	13.7 (8.8-18.5)	13.7 (2.5-24.9)	13.6 (7.9-19.3)	0.03	0.7231
Ig replacement therapy (IGRT)	23(74%)	4(67%)	19(76%)	0.6316	0.6344
IGRT duration	8.1 (4.8-11.4)	8.0 (-3.4-19.4)	8.1 (4.5-11.8)	-0.1	0.9863
Infections	29(94%)	6(100%)	23(92%)	Infinity	>0.9999
Autoimmunity	19(61%)	3(50%)	16(64%)	0.5625	0.6526
Splenomegaly	12(39%)	4(67%)	8(32%)	4.25	0.1735
Granulomatosis	6(19%)	0(0%)	6(24%)	0	0.1815
Malignancies	6(19%)	2(33%)	4(16%)	2.625	0.3345
Lymphadenomegaly	12(39%)	3(50%)	9(36%)	1.778	0.6526
Lung involvement	13(42%)	3(50%)	10(40%)	1.500	0.6758
Atopy	10(32%)	0(0%)	10(40%)	0	0.1411
Blood EBV replication	6(19%)	3(50%)	2(8%)	11.5	**0.0376**
IMMUNOGLOBULINS					
IgG (onset) (g/L)	3.1 (2.3-4.0)	3.6 (1.7-5.5)	3.1 (2.1-4.0)	0.5	0.6446
IgA (g/L)	0.48 (-0.02-0.18)	0.35 (0.01-0.69)	0.52 (-0.11-1.14)	-0.17	0.2023
IgM (g/L)	0.38 (0.18-0.59)	0.36 (-0.07-0.80)	0.39 (0.14-0.63)	-0.03	0.8171
IgE (kU/L)	10.1 (2.7-17.5)	8.7 (-8.6-26.0)	10.5 (1.6-19.5)	-1.8	0.7787
GENERAL IMMUNOPHENOTYPE (ABSOLUTE COUNT: CELLS/ µL)					
Lymphocytes	2118 (1698-2538)	2262 (683-3841)	2084 (1638-2529)	178	0.865
Lymphocytes (% of WBC)	35.3 (31.2-39.5)	35.6 (20.1-51.0)	35.3 (30.9-39.8)	0.2	0.789
Monocytes	369 (306-432)	426 (205-646)	356 (288-423)	70	0.575
Monocytes (% of WBC)	6.3 (5.3-7.2)	6.5 (5.4-7.7)	6.2 (5.0-7.4)	0.3	0.227
T cells	1446 (1177-1716)	1663 (510-2815)	1395 (1130-1659)	268	0.715
T Lymphocytes (% of Lymphocytes)	69.3 (65.4-73.2)	73.3 (65.9-80.8)	68.3 (63.6-73.0)	5.0	0.339
B cells	266 (155-378)	243 (-81-566)	263 (139-387)	-21	0.827
B cells (% of Lymphocytes)	10.9 (7.9-13.8)	9.0 (3.3-14.6)	11.3 (7.8-14.8)	-2.4	0.643
NK cells	172 (121-222)	145 (55-235)	178 (117-240)	-34	0.942
NK cells (% of Lymphocytes)	8.6 (6.5-10.7)	7.8 (2.6-13.0)	8.8 (6.4-11.2)	-1.0	0.751
NKT-LIKE	58 (31-85)	77 (-44-199)	53 (28-79)	24	0.827
NKT-LIKE cells (% of Lymphocytes)	2.7 (1.8-3.6)	2.6 (0.4-4.7)	2.7 (1.6-3.8)	-0.2	0.865
Lineage negative (Lin-)	173 (134-211)	176 (63-288)	172 (128-215)	4	0.935
Lin- cells (% of lymphocytes)	9.4 (7.3-11.5)	9.8 (4.2-15.3)	9.3 (6.9-11.7)	0.4	0.715

B CELLS IMMUNOPHENOTYPE (% OF TOTAL B CELLS)					
Naïve	54.4	61.3	53.1	-8.2	0.5540
IgM$^+$IgD^{++}CD38$^+$CD27$^-$CD21$^+$	(46.3-62.6)	(46.2-66.3)	(43.6-62.7)		
CD21low	9.4	11.2	8.9	-2.3	0.9133
IgM$^+$IgD$^+$CD38^{low}CD27$^-$CD21^{low}	(5.3-13.5)	(-6.2-28.6)	(4.8-13.1)		
Class-switched memory	4.1	1.5	4.7	3.2	0.5995
IgM$^-$IgD$^-$CD38$^+$CD27$^+$CD21$^+$	(1.6-6.6)	(0.2-2.8)	(1.7-7.8)		
Non-switched memory	8.3	3.3	9.5	6.2	0.5168
IgM^{++}IgD$^+$CD38$^+$CD27$^+$CD21$^+$	(4.1-12.5)	(1.3-5.3)	(9.3-14.6)		
Transitional	7.6	6.2	7.9	1.7	0.1459
IgM^{++}IgD^{++}CD38^{++}CD27$^-$CD21$^+$	(3.2-12.0)	(4.0-8.4)	(2.3-13.5)		
Plasmablasts	0.37	0.87	0.25	-0.63	0.0627
IgM$^{-/+}$IgD$^-$CD38^{+++}CD27^{++}CD21$^+$	(0.05-0.69)	(-0.61-2.35)	(-0.03-0.52)		
T CELLS IMMUNOPHENOTYPE					
αβ T cells	1409	1631	1356	275	0.751
	(1145-1673)	(480-2782)	(1101-1611)		
αβ T cells	97.4	97.8	97.4	0.5	0.339
(% of T cells)	(96.8-98.1)	(95.9-99.7)	(96.7-98.1)		
γδ T cells	37.1	31.8	38.4	-6.5	0.715
	(24.8-49.4)	(2.6-61.1)	(23.9-52.9)		
γδ T cells	2.6	2.2	2.6	-0.4	0.364
(% of T cells)	(1.9-3.2)	(0.3-4.1)	(1.9-3.3)		
αβ CD4+ T	805	743	819	-76	0.608
	(667-942)	(323-1164)	(664-975)		
αβ CD4+ T	58.7	49.4	61.1	-11.7	0.067
(% of αβ T cells)	(54.4-63.2)	(33.0-65.8)	(56.8-65.3)		
αβ CD8+ T	528	781	467	314	0.247
	(384-672)	(66-1497)	(353-582)		
αβ CD8+ T	35.7	43.9	33.7	10.3	0.053
(% of αβ T cells)	(31.6-39.7)	(29.6-58.3)	(29.8-37.6)		
αβ DN T cells	68.0	89.0	62.9	26	0.268
	(48.5-87.4)	(33.6-144.5)	(41.1-84.7)		
αβ DN T cells	5.0	6.1	4.8	1.3	0.364
(% of αβ T cells)	(3.9-6.1)	(2.3-9.8)	(3.6-5.9)		
αβ CD4+CD8+ T	8.5	17.0	6.4	10.6	0.903
	(2.6-14.3)	(-17.3-51.3)	(2.9-10.0)		
αβ CD4+CD8+ T	0.52	0.62	0.50	0.12	0.679
(% of αβ T cells)	(0.24-0.80)	(-0.22-1.47)	(0.18-0.81)		
αβ CD4+DR+ T	36.1	32.8	36.9	-4.1	0.865
	(27.6-44.5)	(11.4-54.1)	(27.0-46.8)		
αβ CD4+DR+ T	5.1	5.3	5.0	0.3	0.751
(% of CD4 αβ T cells)	(3.9-6.2)	(2.0-8.6)	(3.7-6.3)		
αβ CD4+CD69+ T	11.6	10.4	11.9	-1.6	0.942
	(8.2-15.1)	(2.2-18.6)	(7.9-16.0)		
αβ CD4+CD69+ T	1.6	1.7	1.5	0.1	0.478
(% of CD4 αβ T cells)	(1.0-2.1)	(0.5-2.8)	(0.9-2.2)		
αβ CD4+DR+CD69+ T	1.1	1.5	1.0	0.5	0.827
	(0.6-1.6)	(-0.8-3.8)	(0.5-1.4)		
αβ CD4+DR+CD69+ T	0.2	0.2	0.1	0.1	0.339
% of CD4 αβ T cells	(0.1-0.2	(0.1-0.5)	(0.07-0.2)		
αβ CD4+DR+CD38+ T	13.8	16.7	13.1	3.6	0.510
	(8.9-18.8)	(-0.4-33.8)	(7.7-18.5)		
αβ CD4+DR+CD38+ T	2.1	2.8	1.9	0.9	0.643
(% of CD4 αβ T cells)	(1.4-2.8)	(0.2-5.4)	(1.1-2.6)		
αβ CD4+CD38+CD69+ T	4.6	5.7	4.4	1.4	0.364
	(3.0-6.3)	(0.2-11.2)	(2.6-6.1)		
αβ CD4+CD38+CD69+ T	0.6	0.8	0.6	0.2	0.247
(% of CD4 αβ T cells)	(0.4-0.8)	(0.3-1.3)	(0.4-0.7)		
αβ CD8+DR+ T	32.2	39.9	30.3	9.5	0.105
	(22.1-42.3)	(21.5-58.3)	(18.2-42.5)		
αβ CD8+DR+ T	6.9	7.6	6.7	0.9	0.510
(% of CD8 αβ T cells)	(5.3-8.4)	(3.5-11.8)	(4.9-8.5)		
αβ CD8+CD69+ T	22.1	26.1	21.2	4.9	0.247
	(6.7-37.6)	(-3.2-55.4)	(2.5-39.9)		
αβ CD8+CD69+ T	4.3	3.2	4.5	-1.3	0.227
(% of CD8 αβ T cells)	(1.3-7.3)	(2.3-4.2)	(0.8-8.3)		
αβ CD8+DR+CD69+ T	1.6	2.4	1.4	0.9	0.208

	(1.1-2.1)	(0.2-4.6)	(0.9-1.9)		
αβ CD8+DR+CD69+ T	0.4	0.5	0.3	0.2	0.391
(% of CD8 αβ T cells)	(0.3-0.5)	(0.1-1.0)	(0.2-0.4)		
αβ CD8+DR+CD38+ T	13.5	19.2	12.1	7.0	0.130
	(8.2-18.8)	(3.7-34.6)	(6.2-18.1)		
αβ CD8+DR+CD38+ T	2.7	3.2	2.5	0.6	0.478
(% of CD8 αβ T cells)	(1.9-3.4)	(0.8-5.5)	(1.7-3.3)		
αβ CD8+CD38+CD69+ T	3.8	9.0	2.6	6.4	0.105
	(1.5-6.1)	(-3.6-21.5)	(1.3-3.9)		
αβ CD8+CD38+CD69+	0.7	0.9	0.6	0.3	0.095
(% of CD8 αβ T cells)	(0.4-0.9)	(0.4-1.4)	(0.3-0.9)		

NK IMMUNOPHENOTYPE (% OF TOTAL NK CELLS)

NK CD56dim	157.3	117	167	-50	0.715
	(108.4-206.2)	(28-206)	(108-226)		
NK CD56dim %	90.6	83.7	92.2	-8.5	0.751
	(86.4-94.8)	(57-111)	(91-94)		
NK CD56bright	10.3	7.2	11.0	-3.8	0.391
	(7.8-12.8)	(4.2-10.2)	(8.0-14.1)		
NK CD56bright %	7.31	5.6	7.7	-2.2	0.208
	(6.11-8.51)	(3.7-7.5)	(6.3-9.1)		
NK DR+	16.7	10.4	18.2	-7.8	0.268
	(11.8-21.5)	(3.8-16.9)	(12.4-24.0)		
NK DR+ %	13.2	8.0	14.4	-6.4	0.247
	(8.8-17.6)	(3.6-12.4)	(9.1-19.8)		
NK CD69+	9.5	5.4	10.4	-5.0	0.608
	(4.8-14.1)	(0.8-10.0)	(4.7-16.2)		
NK CD69+ %	6.7	3.5	7.5	-4.0	0.751
	(3.4-10.0)	(1.0-6.0)	(3.5-11.5)		
NK DR+CD69+	2.7	1.0	3.1	-2.1	0.679
	(-0.2-5.5)	(0.1-1.8)	(-0.5-6.6)		
NK DR+CD69+ %	2.8	0.7	3.3	-2.6	0.478
	(-0.3-5.8)	(0.01-1.4)	(-0.5-7.1)		

PUTATIVE LYMPHOID PRECURSORS

PUTATIVE CD56-CD16+	11.3	5.7	12.7	-6.9	0.060
PRECURSORS	(7.5-15.1)	(-1.6-13.0)	(8.2-17.1)		
PUTATIVE CD56-CD16+	3.45	2.9	3.6	-0.7	0.227
PRECURSORS%	(2.23-4.67)	(-2.2-8.1)	(2.4-4.8)		
LIN-DNAMbright	9.99	4.4	11.3	-6.9	0.075
	(6.56-13.41)	(-0.13-9.0)	(7.3-15.4)		
LIN-DNAMbright %	3.06	1.6	3.3	-1.79	0.291
	(1.85-4.27)	(0.2-3.0)	(1.9b -4.8)		

Quantitative variables were expressed as means with a 95% confidence interval, while qualitative variables were represented as absolute frequencies with percentages relative to the total of the respective column. OR: odds ratio; MD: mean difference; **P** values were calculated by either unpaired two-tailed Student's t-test or Mann-Whitney u test according to variable distribution and sample size. DN: double negative; Univar.: univariate analysis.

Table S4. Comparison between CVID patients with active CMV/EBV replication vs non-replicating

	Total (31)	CMV/EBV (8)	No-CMV/EBV (23)	OR/ MD	P value (univ.)
SAMPLE DEMOGRAPHICS					
Male	14(45%)	3(38%)	11(48%)	0.6545	0.6980
Female	17(55%)	5(63%)	12(52%)	1.528	0.6980
Age	50.4 (44.1-56.7)	52.4 (38.4-66.3)	49.7 (842.1-57.3)	2.64	0.7142
CLINICAL VARIABLES					
Age at diagnosis	39.0 (32.3-45.8)	40.0 (25.1-54.9)	38.7 (30.5-46.9)	1.304	0.7820
Disease duration	13.7 (8.8-18.5)	13.6 (6.1-21.2)	13.7 (7.4-19.9)	-0.03	0.5265
Ig replacement therapy (IGRT)	26(84%)	7(88%)	19(83%)	1.474	>0.9999
IGRT duration	8.1 (4.8-11.4)	9.6 (2.2-17.0)	7.6 (3.6-11.5)	2.02	0.5205
Infections	29(94%)	8(100%)	21(91%)	Infinity	>0.9999
Autoimmunity	19(61%)	5(63%)	14(61%)	1.071	>0.9999
Splenomegaly	12(39%)	6(75%)	6(26%)	8.500	**0.0316**
Granulomatosis	6(19%)	2(25%)	4(17%)	1.583	0.6344
Malignancies	6(19%)	2(25%)	4(17%)	1.583	0.6344
Lymphadenomegaly	12(39%)	5(63%)	7(30%)	3.810	0.2055
Lung involvement	13(42%)	5(63%)	8(35%)	3.125	0.2285
Atopy	10(32%)	0(0%)	10(43%)	0	**0.0317**
IMMUNOGLOBULINS					
IgG (onset) (g/L)	3.1 (2.3-4.0)	3.1 (1.1-5.0)	3.2 (2.2-4.2)	-0.10	0.9205
IgA (g/L)	0.48 (-0.02-0.18)	0.26 (-0.01-0.53)	0.56 (-0.12-1.24)	-0.30	>0.9999
IgM (g/L)	0.38 (0.18-0.59)	0.28 (-0.05-0.60)	0.42 (0.15-0.69)	-0.14	0.5420
IgE (kU/L)	10.1 (2.7-17.5)	6.5 (-5.57-18.62)	11.6 (1.8-21.5)	-5.1	0.3650
GENERAL IMMUNOPHENOTYPE (ABSOLUTE COUNT: CELLS/ µL)					
Lymphocytes	2118 (1698-2538)	2075 (963-3187)	2133 (1654-2612)	-59	0.520
Lymphocytes (% of WBC)	35.3 (31.2-39.5)	36.5 (26.3-48.8)	35.0 (30.5-39.5)	1.5	0.642
Monocytes	369 (306-432)	368 (194-542)	370 (300-440)	-2	0.981
Monocytes (% of WBC)	6.3 (5.3-7.2)	6.1 (5.2-7.1)	6.3 (5.0-7.7)	-0.3	0.674
T cells	1446 (1177-1716)	1533 (727-2338)	1417 (1130-1703)	116	1.000
T Lymphocytes (% of Lymphocytes)	69.3 (65.4-73.2)	74.2 (68.3-80.0)	67.6 (62.7-72.5)	6.6	0.132
B cells	266 (155-378)	209 (-17-435)	277 (143-410)	-68	0.464
B Lymphocytes %	10.9 (7.9-13.8)	8.3 (4.2-12.5)	11.7 (8.0-15.6)	-3.4	0.464
NK cells	172 (121-222)	124 (54-194)	188 (123-253)	-64	0.520
NK cells (% of Lymphocytes)	8.6 (6.5-10.7)	7.0 (3.1-10.9)	9.2 (6.6-11.7)	-2.1	0.411
NKT-LIKE	58 (31-85)	72 (-13-156)	53 (26-80)	19	0.808
NKT-LIKE cells (% of Lymphocytes)	2.7 (1.8-3.6)	2.7 (1.0-4.4)	2.7 (1.5-3.9)	0.02	0.740
Lineage negative (Lin-)	173 (134-211)	169 (83-256)	174 (128-220)	-4	0.842
Lin- cells (% of lymphocytes)	9.4 (7.3-11.5)	9.6 (5.5.13.8)	9.3 (6.8-11.9)	0.3	0.707

B CELLS IMMUNOPHENOTYPE (% OF TOTAL B CELLS)

Naïve IgM$^+$IgD^{++}CD38$^+$CD27$^-$CD21$^+$	54.4 (46.3-62.6)	60.7 (48.3-73.0)	52.5 (42.1-62.8)	8.2	0.5234
CD21low IgM$^+$IgD$^+$CD38^{low}CD27$^-$CD21^{low}	9.4 (5.3-13.5)	11.1 (-0.6-22.9)	8.8 (4.3-13.3)	2.3	0.5569
Class-switched memory IgM$^-$IgD$^-$CD38$^+$CD27$^+$CD21$^+$	4.1 (1.6-6.6)	2.0 (0.6-3.3)	4.9 (1.6-8.2)	-2.9	0.9735
Non-switched memory IgM^{++}IgD$^+$CD38$^+$CD27$^+$CD21$^+$	8.3 (4.1-12.5)	3.2 (1.6-4.8)	10.0 (4.5-15.6)	-6.8	0.4433
Transitional IgM^{++}IgD^{++}CD38^{++}CD27$^-$CD21$^+$	7.6 (3.2-12.0)	7.4 (3.1-11.7)	7.7 (1.6-13.7)	-0.3	0.0845
Plasmablasts IgM$^{-/+}$IgD$^-$CD38^{+++}CD27^{++}CD21$^+$	0.37 (0.05-0.69)	0.66 (-0.38-1.71)	0.26 (-0.04-0.57)	0.40	0.1648
T CELLS IMMUNOPHENOTYPE					
αβ T cells	1409 (1145-1673)	1503 (701-2307)	1376 (1100-1653)	128	1.000
αβ T cells (% of T cells)	97.4 (96.8-98.1)	98.0 (96.6-99.3)	97.3 (96.5-98.0)	0.7	0.172
γδ T cells	37.1 (24.8-49.4)	28.7 (7.9-49.5)	40.1 (24.4-55.7)	-11	0.492
γδ T cells (% of T cells)	2.6 (1.9-3.2)	2.0 (0.7-3.4)	2.7 (2.0-3.5)	-0.7	0.172
αβ CD4+ T	805 (667-942)	738 (448-1027)	828 (659-997)	-90	0.566
αβ CD4+ T (% of αβ T cells)	58.7 (54.4-63.2)	53.0 (40.5-65.4)	60.8 (56.2-65.4)	-7.8	0.219
αβ CD8+ T	528 (384-672)	679 (172-1186)	476 (352-600)	203	0.437
αβ CD8+ T (% of αβ T cells)	35.7 (31.6-39.7)	41.3 (30.8-51.9)	33.7 (29.4-38.0)	7.7	0.121
αβ DN T cells	68.0 (48.5-87.4)	73.3 (28.7-117.9)	66.1 (42.8-89.4)	7.2	0.947
αβ DN T cells (% of αβ T cells)	5.0 (3.9-6.1)	5.1 (2.2-8.0)	5.0 (3.8-6.2)	0.1	0.877
αβ CD4+CD8+ T	8.5 (2.6-14.3)	13.9 (-9.8-37.5)	6.6 (2.8-10.5)	7.3	1.000
αβ CD4+CD8+ T (% of αβ T cells)	0.52 (0.24-0.80)	0.56 (-0.02-1.15)	0.51 (0.16-0.86)	0.05	0.611
αβ CD4+DR+ T	36.1 (27.6-44.5)	33.8 (17.0-50.6)	36.9 (26.3-47.4)	-3.1	0.912
αβ CD4+DR+ T (% of CD4 αβ T cells)	5.1 (3.9-6.2)	5.4 (2.6-8.2)	5.0 (3.6-6.3)	0.5	0.740
αβ CD4+CD69+ T	11.6 (8.2-15.1)	9.6 (3.9-15.3)	12.3 (7.9-16.8)	-2.7	0.707
αβ CD4+CD69+ T (% of CD4 αβ T cells)	1.6 (1.0-2.1)	1.5 (0.7-2.3)	1.6 (0.9-2.3)	-0.1	0.707
αβ CD4+DR+CD69+ T	1.1 (0.6-1.6)	1.3 (-0.3-2.8)	1.0 (0.5-1.5)	0.3	0.912
αβ CD4+DR+CD69+ T % of CD4 αβ T cells	0.2 (0.1-0.2)	0.20 (-0.01-0.41)	0.14 (0.06-0.21)	0.06	0.437
αβ CD4+DR+CD38+ T	13.8 (8.9-18.8)	19.1 (6.6-31.7)	12.0 (6.4-17.5)	7.2	0.121
αβ CD4+DR+CD38+ T (% of CD4 αβ T cells)	2.1 (1.4-2.8)	3.09 (1.13-5.05)	1.69 (0.98-2.39)	1.40	0.187
αβ CD4+CD38+CD69+ T	4.6 (3.0-6.3)	5.3 (1.4-9.2)	4.4 (2.4-6.3)	0.9	0.386
αβ CD4+CD38+CD69+ T (% of CD4 αβ T cells)	0.6 (0.4-0.8)	0.73 (0.35-1.10)	0.57 (0.37-0.76)	0.16	0.339
αβ CD8+DR+ T	32.2 (22.1-42.3)	37.9 (22.1-53.7)	30.2 (17.2-43.2)	7.7	0.145
αβ CD8+DR+ T (% of CD8 αβ T cells)	6.9 (5.3-8.4)	7.94 (4.01-1.87)	6.50 (4.72-8.29)	1.44	0.386
αβ CD8+CD69+ T	22.1 (6.7-37.6)	22.7 (2.3-43.2)	21.9 (1.5-42.3)	0.8	0.295
αβ CD8+CD69+ T (% of CD8 αβ T cells)	4.3 (1.3-7.3)	3.28 (2.65-3.90)	4.63 (0.52-8.74)	-1.35	0.091
αβ CD8+DR+CD69+ T	1.6 (1.1-2.1)	2.2 (0.6-3.7)	1.4 (0.9-2.0)	0.8	0.187

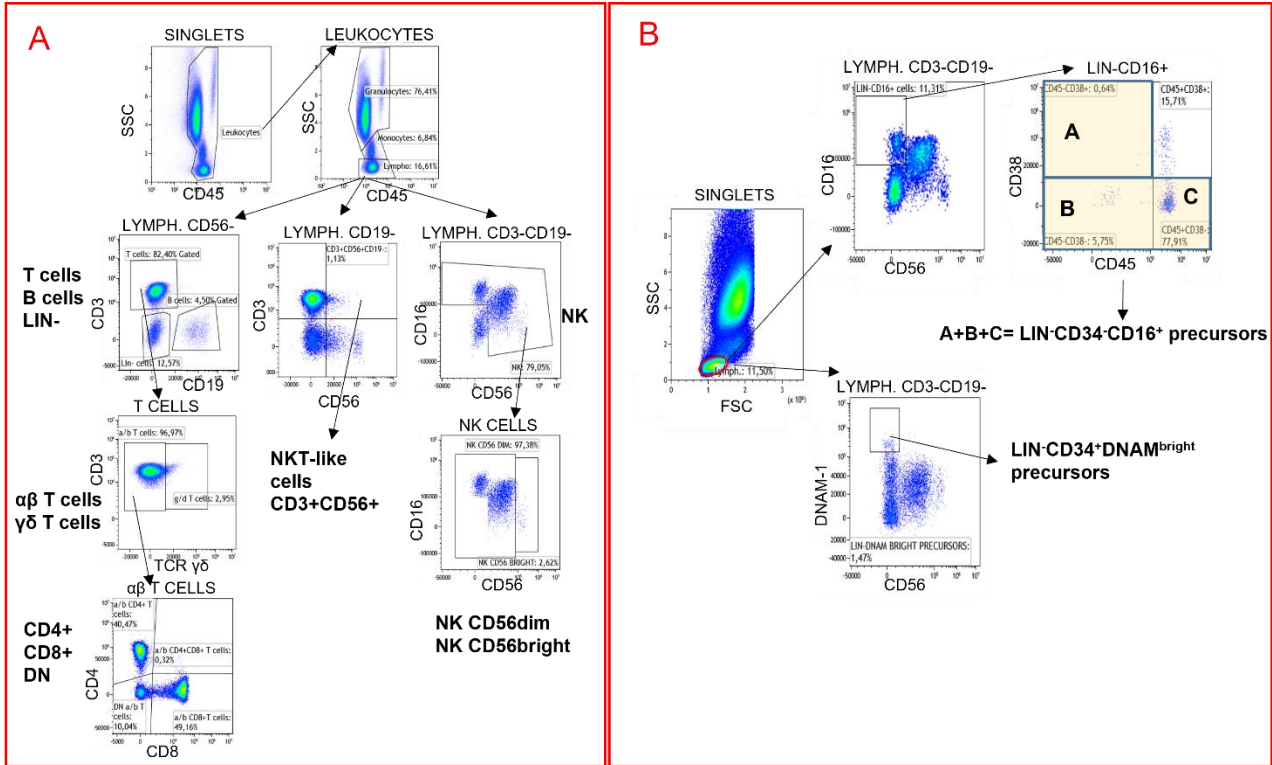|					
αβ CD8+DR+CD69+ T (% of CD8 αβ T cells)	0.4 (0.3-0.5)	0.49 (0.17-0.80)	0.32 (0.21-0.43)	0.16	0.275
αβ CD8+DR+CD38+ T	13.5 (8.2-18.8)	18.3 (6.7-29.9)	11.9 (5.5-18.2)	6.4	0.082
αβ CD8+DR+CD38+ T (% of CD8 αβ T cells)	2.7 (1.9-3.4)	3.46 (1.28-5.63)	2.38 (1.64-3.11)	1.08	0.295
αβ CD8+CD38+CD69+ T	3.8 (1.5-6.1)	7.1 (-1.8-16.1)	2.6 (1.2-4.1)	4.5	0.158
αβ CD8+CD38+CD69+ (% of CD8 αβ T cells)	0.7 (0.4-0.9)	0.77 (0.38-1.16)	0.62 (0.31-0.93)	0.15	0.121
NK IMMUNOPHENOTYPE (% OF TOTAL NK CELLS)					
NK CD56^{dim}	157.3 (108.4-206.2)	102.0 (36.4-167.6)	176.6 (114.3-238.9)	-74.6	0.317
NK CD56^{dim} %	90.6 (86.4-94.8)	85.8 (67-4-104.2)	92.2 (90.7-93.7)	-6.4	0.877
NK CD56^{bright}	10.3 (7.8-12.8)	6.5 (4.1-8.8)	11.6 (8.4-14.8)	-5.2	0.082
NK CD56^{bright} %	7.31 (6.11-8.51)	6.2 (4.4-7.9)	7.7 (6.2-9.2)	-1.6	0.362
NK DR+	16.7 (11.8-21.5)	9.4 (4.7-14.2)	19.2 (13.0-25.4)	-9.8	0.074
NK DR+ %	13.2 (8.8-17.6)	9.0 (5.5-12.4)	14.7 (8.8-20.5)	-5.7	0.492
NK CD69+	9.5 (4.8-14.1)	4.8 (1.5-8.0)	11.1 (4.9-17.3)	-6.4	0.464
NK CD69+ %	6.7 (3.4-10.0)	4.2 (1.7-6.7)	7.6 (3.2-12.0)	-3.4	0.947
NK DR+CD69+	2.7 (-0.2-5.5)	0.8 (0.1-1.4)	3.3 (-0.6-7.2)	-2.5	0.674
NK DR+CD69+ %	2.8 (-0.3-5.8)	0.6 (0.1-1.2)	3.5 (-0.6-7.7)	-2.9	0.642
PUTATIVE LYMPHOID PRECURSORS					
PUTATIVE CD56-CD16+ PRECURSORS	11.3 (7.5-15.1)	5.10 (0.07-10.12)	13.47 (8.81-18.13)	-8.4	**0.012**
PUTATIVE CD56-CD16+ PRECURSORS%	3.45 (2.23-4.67)	2.65 (-0.89-6.19)	3.73 (2.43-5.02)	-1.07	0.145
LIN-DNAM^{bright}	9.99 (6.56-13.41)	3.90 (0.72-7.07)	12.10 (7.86-16.34)	-8.2	**0.034**
LIN-DNAM^{bright} %	3.06 (1.85-4.27)	1.51 (0.53-2.50)	3.60 (2.02-5.17)	-2.09	0.172

Quantitative variables were expressed as means with a 95% confidence interval, while qualitative variables were represented as absolute frequencies with percentages relative to the total of the respective column. P values were calculated by either unpaired two-tailed Student's t-test or Mann-Whitney u test according to variable distribution and sample size. OR: odds ratio; MD: mean difference; DN: double negative; Univ.: univariate analysis. MAPO

Supplementary figure

Fig. S1

Legend to supplementary figure

Fig. S1: **Gating strategy. A.** Leukocyte population gating strategy (CD45/SSc). **B**. Side Scatter/Forward Scatter gating strategy to identify inflammatory lymphoid precursors (LIN-CD34-CD16+, LIN-CD34+DNAMbright). Abbreviations: DN: double negative; FSC: forward scatter; LIN: lineage; Lymph.: lymphocytes; SSC: side scatter.