

Supplemental Table 1. Clinical Information

Sample	Gender	Organ(s) Transplanted	Age at Transplant (Months)	Time from Transplant to PTLD Diagnosis (Months)	Time from Transplant to Sample Blood Draw (Months)
EBV-Low1	M	Liver	7 months	NA	2 months
EBV-Low2	M	Liver; Liver	8 months; 21 months	NA	93 months; 80 months
EBV-Low3	M	Liver	1 month	NA	4 months
EBV-Low4	M	Liver	5 months	NA	55 months
EBV-Low5	M	Liver; Liver	7 months; 7 months	NA	23 months; 23 months
EBV-Low6	M	Liver	5 months	NA	50 months
EBV-High1	F	Liver	6 months	NA	54 months
EBV-High2	F	Liver	6 months	NA	43 months
EBV-High3	F	Liver; Liver	6 months; 7 months	NA	21 months; 21 months
EBV-High4	F	Liver; Liver	84 months; 168 months	NA	36 months
EBV-High5	F	Liver	6 months	NA	11 months
EBV-High6	M	Liver	9 months	NA	32 months
PTLD1	F	Liver	8 months	5 months	5 months
PTLD2	M	Liver	0 months	55 months	55 months
PTLD3	M	Liver	6 months	7 months	7 months
PTLD4	M	Liver and Kidney	20 months	Unknown	6 months
PTLD5	M	Liver	15 months	6 months	6 months
PTLD6	M	Liver	14 months	42 months	42 months

Supplemental Table 2. Primers for EBV Enrichment

Name	Type	Sequence	Product Size
A	Forward Primer	CTCAGTCACGGGACATTAAC	1501
	Reverse Primer	AGTAGAGTGGGAGTGCTATC	
B	Forward Primer	GCTTCTACAGGACCATCAAC	1084
	Reverse Primer	CCCTGTTCTCCCAATGTAATC	
C	Forward Primer	GACAAAGGACGAGGTAGATAAC	1673
	Reverse Primer	GCCCTTAGACTTACGGTTTAG	
D	Forward Primer	CACCTACCGGATGATGTTAAG	1642
	Reverse Primer	CTGCCAGTGCTTCGTTATAG	
E	Forward Primer	CCGTGTCCACTCACATATTC	1485
	Reverse Primer	CTACTTCTTCTCTGCTCGTTAC	
F	Forward Primer	GGGAAATGAGGGTTAGCATAG	2303
	Reverse Primer	GAACAGTAAGGTGTATGTGAGG	
G	Forward Primer	GTAACGAGCAGAGAAGAAGTAG	2126
	Reverse Primer	CTCTGATGCGACCAGAAATAG	
H	Forward Primer	GGAACCTGGTCATCCTTTG	1353
	Reverse Primer	GAACTCCAGATGGGTGTATTG	
I	Forward Primer	AGCCTATGCTACCCAGATATAG	2247
	Reverse Primer	GCTTCCAGGGTATGGAATTATC	
J	Forward Primer	GGTGGCAGCCTGTTTATAG	1827
	Reverse Primer	GGTCGTGTTGGTGGAATAG	
K	Forward Primer	CACGGATAGTCTTGGAACC	1376
	Reverse Primer	GTCCCTCCACATAATCTTCATC	
L	Forward Primer	AATGTTAGGTCTGCTTTAGGG	1155
	Reverse Primer	CCGAGGGTAGATGATGTAATTG	
M	Forward Primer	GCGGGTCATGGATATGATTAG	1334
	Reverse Primer	TCAGAGACGGCAGGTATAG	
N	Forward Primer	GTGTGGGAAGATGGGAATAC	1117
	Reverse Primer	CATGTGCCTCAGGAGTTTAG	
O	Forward Primer	GGATCTGAGCTATGTGGAATG	1094
	Reverse Primer	ACTGGAGAGTGGGTCTAAAG	
P	Forward Primer	GGGCATAGTCCTCAAAGAAG	1730
	Reverse Primer	GTCCACCTCAGAAACATCAG	
Q	Forward Primer	GAGCAGGAGATGCATGATTAG	2446
	Reverse Primer	GTGGATCATAGGCGAGAAAC	
R	Forward Primer	TTTCGTGGCGATCGTAAG	1389
	Reverse Primer	GAACAGGACCTGCGTTATAG	
S	Forward Primer	CTCCTTGTCTTCCTGTTCTC	1057
	Reverse Primer	CCTTAGTGATATGAGCGGTATC	

T	Forward Primer	CATCTCCCGTTGTTCCAATAG	2343
	Reverse Primer	CTCAAGCGACAGTATGAGAAG	
U	Forward Primer	GGAGTGCCATAAGGCATAAG	1019
	Reverse Primer	CCCGTCTACCACAAC TTTC	
V	Forward Primer	TCACGATAGAGGTGGTCTATG	1121
	Reverse Primer	GATGCCGGTGCTAAGATG	
W	Forward Primer	GTCCATCTCAGGAGTCTCTAT	1798
	Reverse Primer	CTTTGGCCTCGTCCTATTC	
X	Forward Primer	GCCATAGTGTTCAGCATAA	1040
	Reverse Primer	AGGAGGAGAAGGAGCATAC	
Y	Forward Primer	CTGAGGAGTTCGGATGAAAG	1968
	Reverse Primer	CAGGGAGAGAGGAGTGAATA	
Z	Forward Primer	GGATGTGCGAGCCATAAA	1784
	Reverse Primer	GTAGACTCTGAGGGAGAAGAA	
AA	Forward Primer	TTCCCTCTTCCCTTGTTATTC	2468
	Reverse Primer	TACCTAGAGGCCATGCTATT	
AB	Forward Primer	GGGTCCTCTGGATTAGATAGT	2199
	Reverse Primer	GACCAGTCTGGGAGATAGAA	
AC	Forward Primer	GGGATTGGAAGTGTGCTATAA	1051
	Reverse Primer	CCAGAAACCTGAGCAAGTAG	
AD	Forward Primer	CAAGTCCCTGATGTTCTCTATC	2027
	Reverse Primer	GCAGCTCATCCCTACTTATG	
AE	Forward Primer	TCCTCTCTCCCTGTTTATCC	2406
	Reverse Primer	CCTGGTGTGAAGTCCAATC	
AF	Forward Primer	GCCGTTGGATCTTAGTGTTAT	1526
	Reverse Primer	GGTTCATTTCTCCCGTTAG	
AG	Forward Primer	GTGTGTCCAGTGCCTAATC	1543
	Reverse Primer	CAGAGGAGGAGGATGAAGAT	
AI	Forward Primer	CGATCTAGGTAGGTGGATAGAC	1380
	Reverse Primer	CATGCAGGGTATTCTAGTGAAG	
AJ	Forward Primer	TCTTCCACGAAGGCAAAG	1340
	Reverse Primer	TAGGTCAGAGCGACATAGAG	
AK	Forward Primer	CGCCATCCTCCATAATACAC	1948
	Reverse Primer	TCCACCTCTGGACACTATAC	
AL	Forward Primer	GTGAGCGGAGGTTAGTAAAG	1734
	Reverse Primer	GGAGAGGAGCAACAAGTAAG	
AM	Forward Primer	CTGATAATACGCCGACAATAA	2260
	Reverse Primer	GGTGTAGGCTGATATGGAATG	
AN	Forward Primer	GGACCAGTTCTACTCCTACA	1517
	Reverse Primer	ACCACAGGCCAACATAAC	

AO	Forward Primer	CTATGGCCTAAGTGTGTGATG	2240
	Reverse Primer	GCCTGGCTGAGATGATATTG	
AP	Forward Primer	GGTGAAACGCGAGAAGAA	2498
	Reverse Primer	CGGTCATGCACATCCATATAA	
AQ	Forward Primer	GAGGTGTTGTGTCCTGTATG	1642
	Reverse Primer	CTCGTCCTCATCACCAATTAC	
AR	Forward Primer	AGTCTGTTGATTCTGGGTATG	2420
	Reverse Primer	CGGGATAGTGTTCAGGTAAAG	
AS	Forward Primer	GGCGCGTTGTTGTTATTG	2342
	Reverse Primer	CCTCGCCTTAGGTTGTAAAG	
AT	Forward Primer	CCTTGAAC TTGGAGCTTAGG	2174
	Reverse Primer	CACTGCTTAGTGTGTGGTATTA	
AU	Forward Primer	CATCCTGCGTCAACAGATAG	1572
	Reverse Primer	CCTCTTCCATTCCGACATTAG	
AV	Forward Primer	GGAGTAGGAGGTGGGAATAA	1976
	Reverse Primer	ATGCTCTGAAAGACAGGATAAG	
AW	Forward Primer	GGCGACAGTTGAAGAAGTAG	1856
	Reverse Primer	ACTGGAAGGGTGAGGATATAG	
AX	Forward Primer	CTGACCGAGAACCTAAGAAAC	1166
	Reverse Primer	CAACGACTACGTACCCATAAC	
AY	Forward Primer	GCCACCTGCTTCAATAAGA	1970
	Reverse Primer	GAGATAACGCAAGAGGAGAATAG	
AZ	Forward Primer	GACCGCAACCGTCTATTT	1411
	Reverse Primer	GGCATCTTCCTCCTTGTTTAG	
BA	Forward Primer	GAAAGAGAGGCTGGAAGATG	1613
	Reverse Primer	GAGGAAGATGAGGACGTAGA	
BB	Forward Primer	GCCCATCTTCTGGTACATTC	2015
	Reverse Primer	CCCATCTCCACAAATCACTAC	
BC	Forward Primer	TTACTGCGCGGATCTAAAC	2046
	Reverse Primer	CATCTTCCAGCCTCTCTTTC	
BD	Forward Primer	GCAGATACTCGCAGGTAATG	2467
	Reverse Primer	TTTCCCACTGTGCCTAAAC	
BE	Forward Primer	CACCAATGACGGCCTAAA	1291
	Reverse Primer	GATGAGATAGCCCGGATAGA	
BF	Forward Primer	TTGATTCTGATCCTGGGTATTG	2479
	Reverse Primer	GATGTTGCCACCTTTGTTATG	
BG	Forward Primer	CGTTCACCGTCAGTCTATTC	2235
	Reverse Primer	CAACCTCCACGTTCACTATC	
BH	Forward Primer	GACAGCGCAGCTGATAAA	1476
	Reverse Primer	TGTGACCCACCTAACAATC	

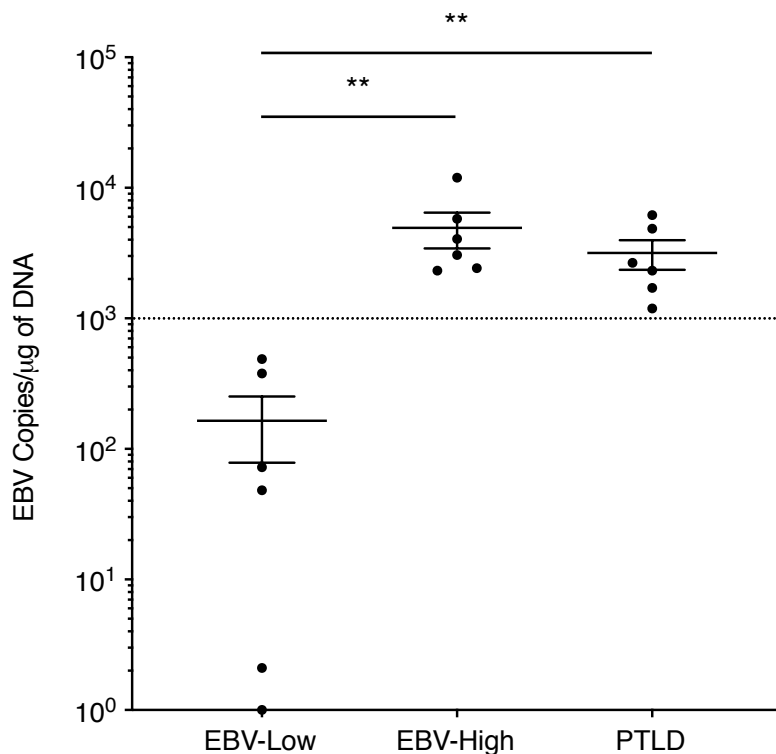
BI	Forward Primer	TCGGTTCAGGGACTACAA	1253
	Reverse Primer	GCTCATGGCCGTCTTAAA	
BJ	Forward Primer	GACCCACGTTTACAGACTTTAG	2157
	Reverse Primer	CCCGTGCGATGAGTTTATT	
BK	Forward Primer	GGGAGGTGATGTAGGTTGTA	1725
	Reverse Primer	CCGAAGATTTGGCGTCTATG	
BL	Forward Primer	CCAACTCCGTCTCCCTAAA	2206
	Reverse Primer	CGCTGACTCTGTGCAATATC	
BM	Forward Primer	TGGTAGTGGCTGGGATAA	1945
	Reverse Primer	GTCGATGGGCAGCTATATTC	
BN	Forward Primer	CCCACGAGTATCCAGTTCTA	1398
	Reverse Primer	TGTTGCCCTCTCCTCTAAT	
BO	Forward Primer	GGTACCTGGAGGTCATTCTA	2379
	Reverse Primer	GTCTTTCAACGGCAACAATAC	
BP	Forward Primer	GGCAAGCTGTCCTTCTTT	1922
	Reverse Primer	CACCTCCGTCTCTCTGATAA	
BQ	Forward Primer	GTCAGGGAGTCTTGGTAGAA	1632
	Reverse Primer	CGAGCGGAGGATTGTTATTAG	
BR	Forward Primer	CACACCTTCACTCCTTGTTAG	2102
	Reverse Primer	GAGACTGGACCCTACTACTATTC	
BS	Forward Primer	GAAGGCGCTGTAGGATTTAG	2354
	Reverse Primer	AAGAAGGAGGATGTGCATTAC	
BT	Forward Primer	GTAATGCACATCCTCCTTCTT	1830
	Reverse Primer	CTCTGGTTTCATCTCCTTCTTC	
BU	Forward Primer	GGCGTGGCAGAATAGTATAAG	1568
	Reverse Primer	GAATTGGGATGGTGTGGATAA	
BV	Forward Primer	GTACCACCAGGAGTAGTCTTA	1977
	Reverse Primer	CTCCTTGTCTCTATTCTTTG	
BW	Forward Primer	CCAGACTTCTCTGTCCTTACT	1637
	Reverse Primer	GCCTTCTTTCCTTGTCTTAC	
BX	Forward Primer	CGGAAACAACTCCCAATATCC	1483
	Reverse Primer	GACTGACTCTCCCTCCATTTA	
BY	Forward Primer	GCAGAGCCTTGACATTGA	2109
	Reverse Primer	GCCAGAAGCAGATGGATATT	
BZ	Forward Primer	CTACCTGTGTGGTGTGTTAAG	1913
	Reverse Primer	CGCCTCTTTGTGCAGATTA	
CA	Forward Primer	GCCAGAGCATCTCCAATAAG	1480
	Reverse Primer	CCTGTCAATTCTACCCTCCA	
CB	Forward Primer	CCAGTCCAGTCACTCATAAC	1615
	Reverse Primer	CTGTCATTCTACCCTCCAAC	

Supplemental Table 3. HLA Typing

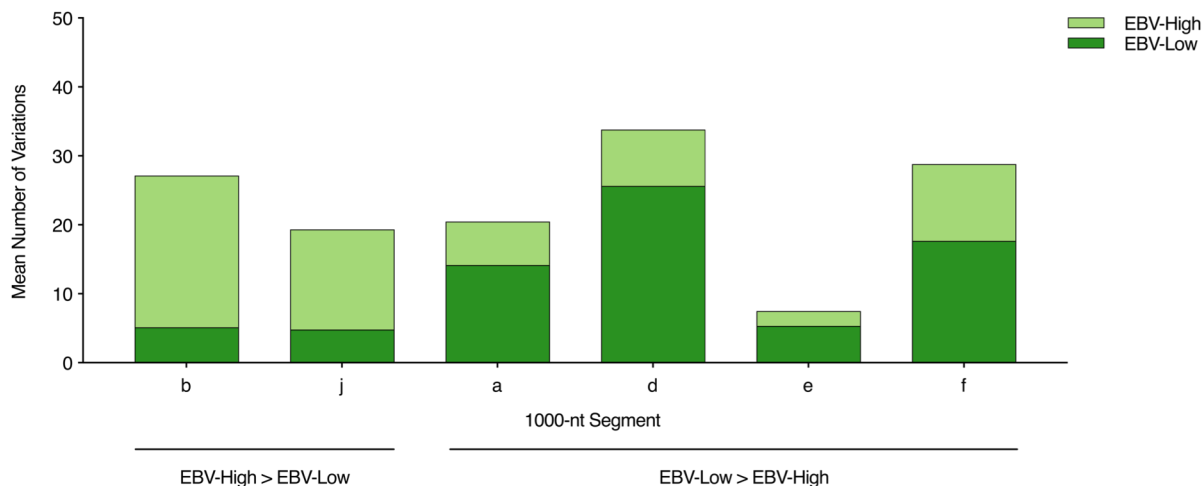
Sample	HLA-A	HLA-B	HLA-DR
EBV-Low1	A*24:02:01:01 A*33:01:01:01	B*52:01:02:01 B*14:02:01:01	DRB1*04:04:01 DRB1*01:02:01
EBV-Low2	*nd	nd	nd
EBV-Low3	A*24:02:01:01 A*02:01:01:01	B*51:01:02 B*47:01:01:03	DRB1*11:01:01:01 DRB1*13:03:01
EBV-Low4	A*23:01:01:01 A*31:02	nd	nd
EBV-Low5	A*01:01:01:01 A*68:01:02:01	B*35:01:01:05 -	DRB1*11:01:01:01 DRB1*01:01:01
EBV-Low6	nd	nd	nd
EBV-High1	A*30:04:01 A*25:01:01:01	B*41:01:01:01 B*18:01:01:05	DRB1*13:05:01 DRB1*15:02:01:01
EBV-High2	A*25:01:01:01 A*24:02:01:01	B*18:01:01:05 B*18:01:01:05	DRB1*15:01:01:01 -
EBV-High3	A*30:01:01 A*03:01:01:01	B*13:02:01:01 B*44:02:01:03	DRB1*07:01:01:01 DRB1*11:01:01:03
EBV-High4	nd	nd	nd
EBV-High5	A*32:01:01:01 A*24:02:01:01	B*14:01:01:01 B*51:01:01:01	nd
EBV-High6	A*02:01:01:01 A*02:01:01:01	B*13:02:01:01 B*47:01:01:03	DRB1*13:01:01:02 DRB1*08:01:01
PTLD1	A*32:01:01:01 A*02:01:01:01	nd	nd
PTLD2	A*02:01:01:01 A*03:01:01:01	B*14:01:01:01 B*37:01:01:01	nd
PTLD3	A*11:01:01:01 -	DRB1*12:01:01:03 DRB1*14:54:01:02	DRB1*12:01:01:03 DRB1*14:54:01:02
PTLD4	A*02:01:01:01 A*01:01:01:01	B*40:01:02:01 B*35:01:01:01	DRB1*04:01:01:03 DRB1*01:01:01:01
PTLD5	nd	nd	nd
PTLD6	A*02:07:01 A*01:01:01:01	B*46:01:01 B*57:01:01:01	DRB1*09:01:02:01 DRB1*07:01:01:02
SLCL 1	A*02:05:01:01 A*01:01:01:01	B*58:01:01:01 B*08:01:01:01	DRB1*15:03:01:01

			DRB1*03:01:01:01
SLCL 2	A*02:01:01:01 A*01:01:01:01	B*40:01:02:01 B*35:01:01:01	DRB1*04:01:01:03 DRB1*01:01:01
SLCL 3	A*02:01:01:01 A*26:01:01:01	B*40:01:02:01 B*50:01:01:01	DRB1*11:01:01:03 DRB1*04:06:02
SLCL 4	A*02:01:01:01 -	B*27:05:02:01 -	DRB1*01:01:01 -
SLCL 5	A*30:01:01:01 A*02:01:01:01	B*41:01:01:01 B*44:03:01:01	DRB1*07:01:01:01 DRB3*03:01:01
SLCL 6	nd	nd	nd

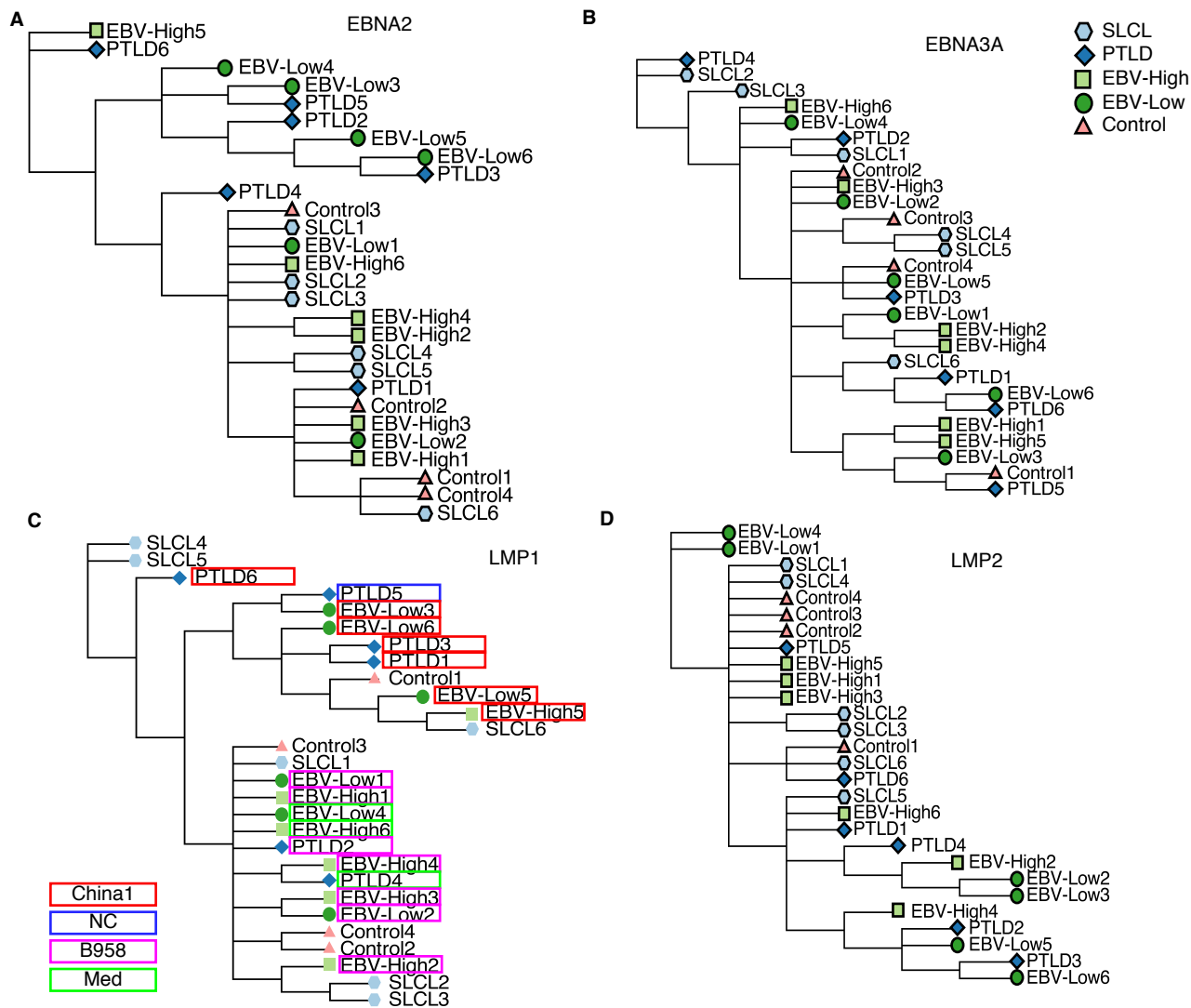
*nd, not done due to insufficient DNA available



Supplemental Figure 1. EBV viral load in transplant patients classified as PTLD, EBV-High, and EBV-Low. EBV viral load quantification was determined using artus EBV PCR kit and 1st WHO International Standard EBV. EBV viral load was calculated as number of copies per microgram of DNA from whole blood. EBV-High is defined as > 1000 copies per μ g of DNA and EBV-Low is defined as ≤ 1000 copies per μ g of DNA. Mean and standard error of the mean are shown for each group. EBV-High and PTLD groups have significantly higher viral load than the EBV-Low group as determined by two-way ANOVA and Tukey's multiple comparisons test. PTLD vs EBV-Low $p=0.004$. EBV-High vs EBV-Low $p=0.01$.



Supplemental Figure 2. Comparison of the number of variations within specific 1000-nt segments in EBV-High and EBV-Low groups. Segment b) located within the BPLF1 gene, EBV-High vs EBV-Low $p=0.04$. Segment j) Includes part of BDLF3 and BDLF2 genes. EBV-High vs EBV-Low $p=0.0003$. Segment a) Includes part of EBNA2 gene; EBV-High vs EBV-Low $p=0.04$. Segment d) Within the EBNA3C gene, EBV-High vs EBV-Low $p=0.03$. Segment e) Within the EBNA3C gene. EBV-High vs EBV-Low $p<0.0001$. Segment f) Within the EBNA3C gene. EBV-High vs EBV-Low $p<0.03$. Statistical significance between number of variations from EBV-High and EBV-Low groups was determined using two-way ANOVA with Tukey's multiple comparisons test.



Supplemental Figure 3. Phylogenetic Analysis of Latent Genes EBNA2, EBNA3A, LMP1, and LMP2. (A) Phylogenetic analysis of EBNA2 genes. (B) Phylogenetic analysis of EBNA3A genes. (C) Phylogenetic analysis of LMP1 genes. LMP1 types China1 (red), NC (blue), B958 (pink), and Med (green) are shown as boxes around the samples for the PTLD, EBV-High, and EBV-Low groups. (D) Phylogenetic analysis of LMP2 genes. (A-D) Light blue hexagons=SLCL samples, dark blue diamonds=PTLD samples, light green squares=EBV-High samples, dark green circles=EBV-Low samples, and pink triangles=Control samples. Nucleotide sequences were aligned using MUSCLE alignment. Trees were constructed using neighbor-joining model and Jukes-Cantor genetic distance modeling.