

Supplementary Materials: Complete Genome Sequence of Germline Chromosomally Integrated Human Herpesvirus 6A and Analyses Integration Sites Define a New Human Endogenous Virus with Potential to Reactivate as an Emerging Infection

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Table S1. Geographic prevalence studies separated into CiHHV-6A and CiHHV-6B.

Study	Country	n	CiHHV-6A (%)	CiHHV-6B (%)	References
Donors					
Cord blood	USA (NY)	5638	[19 *] 12 (0.2)	[38 *] 25 (0.4)	(Hall <i>et al.</i> , 2008, 2004)
Blood donor-adult	USA (Texas)	100	0 (<1.0)	1 (1.0)	(Hudnall <i>et al.</i> , 2008)
Blood donor	Canada (Ontario)	288	0 (<0.3)	0 (<0.3)	(Gravel <i>et al.</i> , 2013)
Blood donors-adult	France	200	0 (<0.5)	1 (0.5)	(Geraudie <i>et al.</i> , 2012)
Blood donor-adult	UK (London)	500	0 (<0.2)	4 (0.8)	(Leong <i>et al.</i> , 2007)
Serum bank-child	UK	610	4 + (0.7)	6 + (1.0)	(Ward <i>et al.</i> , 2005)
Blood controls	UK (Northern)	563	1 (0.2)	10 (1.7)	(Bell <i>et al.</i> , 2014) ^
Nails adult	Czech Republic	421	1 (0.2)	3 (0.7)	(Hubacek <i>et al.</i> , 2013)
Normal birth/infant-saliva, sera, nails	Southern Africa (Zambia)	495	0 (<0.2)	0 (<0.2)	#
Region Totals	North America N	6026	12 (0.2)	26 (0.4)	
	Europe E	2582	6 (0.2)	24 (0.9)	
Donor Total	NA + E	8608	18 (0.2)	50 (0.6)	
Patients					
SOT-Liver	USA	548	1 (0.2)	6 (1.1)	(Lee <i>et al.</i> , 2012)
SOT-Kidney	USA	46	0 (<2.0)	1 (2.2)	(Lee <i>et al.</i> , 2011)
Leukemic children	Canada (Ontario)	287	1 (0.3)	0 (<0.3)	(Gravel <i>et al.</i> , 2013)
SOT-mixed. Blood, tissue, hair samples	Italy	135	1 (0.7)	0 (<0.8)	(Potenza <i>et al.</i> , 2009)
SCT-Blood, hair samples	Italy	70	0 (<1.4)	1 (1.4)	(Potenza <i>et al.</i> , 2009)
CSF-encephalitis referral child/adult	UK	522	1 (0.2)	5 (1.0)	(Ward <i>et al.</i> , 2007)
Hodgkins lymphoma	UK (Northern)	936	1 (0.1)	15 (1.6)	(Bell <i>et al.</i> , 2014) ^
Cardiac referrals	Germany	3610	7 (0.2)	13 (0.4)	(Tweedy <i>et al.</i> , 2015)
Malignant disease-blood	Czech Republic	812	7 (0.9)	2 (0.2)	(Hubacek <i>et al.</i> , 2013)
Leukemia-child-blood	Czech Republic	339	4 (1.2)	1 (0.3)	(Hubacek <i>et al.</i> , 2009)
Transplant donors/recipients-blood, herpesvirus referrals	Japan (Osaka)	2332	1 (0.04)	4 (0.2)	(Tanaka-Taya <i>et al.</i> , 2004)
Neonatal intensive care unit, sera	Southern Africa (Zambia)	303	0 (<0.3)	0 (<0.3)	(Tembo <i>et al.</i> , 2014) ^
Leukemia-blood	North Africa (Tunisia)	73	0 (<1%)	1 (1.2%)	(Faten <i>et al.</i> , 2012)
	North America	881	2 (0.2)	7 (0.8)	
Region Totals	Europe	6424	21 (0.3)	37 (0.6)	
	Japan, J	2332	1 (0.04)	4 (0.2)	
Patient Total	NA + E + J + A	9719	23 (0.3)	34 (0.4)	

Table S1. Cont.

Study	Country	n	CiHHV-6A (%)	CiHHV-6B (%)	References
Donor + Patients					
Region Totals	North America	6907	14 (0.2)	33 (0.5)	
	Europe	9006	27 (0.3)	61 (0.7)	
	Japan	2332	1 (0.04)	4 (0.2)	
	Africa, A	868	0 (<0.1)	1 (0.1)	
ALL	NA + E + J + A	19,113	41 (0.2)	74 (0.4)	

* Original numbers screened, then those positively identified listed next; +4 and 6 positively identified; SOT—solid organ transplantation recipients; CSF—cerebral spinal fluid; NA North America; # Musonda, K. and Gompels, U.A., Analyses congenital infections with betaherpesviruses in Zambia, unpublished; manuscript in preparation; ^ References [1,15] type by polymerase gene, which HHV-6A variation may confound [4,16].

Table S2. HHV-6A SNPs detected in CiHHV-6A by deep sequencing.

No.	SNPs U54 HHV-6A > CiHHV-6A	SNPs U54 Amino Acid	HHV-6A U1102	% HHV-6A Minor Variant SNPs in CiHHV-6A		
	HHV-6A:U1102, GS & AJ	Changes	Position	2284	5055	5814
1	A > G	-	86,106	<	<	<
2	A > G	-	86,142	17	<	<
3	G > A (AJ only)	-	86,195	17	<	<
4	A > G (AJ only)	I > T	86,329	16	<	<
5	G > T (AJ only)	L > I	86,372	16	<	<
6	T > C	[S, A, T > M]	86,379	17	<	<
7	G > A	[S, A, T > M]	86,380	18	<	<
8	C (U1102) A (GS) > T	S, A, T > M	86,381	<	<	<
9	T > C	T > A	86,387	16	<	<
10	G > C	-	86,400	17	<	<
11	T > C (GS only)	-	86,514	14	<	<
12	T > C	T > A	86,537	30	<	4
13	G > T	T > N	86,608	31	<	<
14	A > G	-	86,613	31	<	<
15	A > G	-	86,619	31	<	<
16	C > A	V > F	86,627	30	<	<
17	G > A	-	86,638	28	<	<
18	G > A	P > S	86,645	25	<	<
19	A > G	-	86,720	17	<	<
20	T > A (GS only)	-	86,724	<	<	<
21	G > T	A > D	86,761	16	<	<
22	A > C	[I, L > R]	86,791	17	<	<
23	T > G (GS only)	I, L > R	86,792	<	<	<
24	T > C (AJ only)	N > D	86,801	17	<	<
25	G > T (U1102)	K, N > I	86,811	<	<	<
26	T > A	[K, N > I]	86,812	16	<	<
27	A > G	-	86,859	14	<	<
28	T > C	N > D	86,891	19	<	<
29	C > G (U1102 only)	G > A	86,893	<	<	<
30	G > T	T > N	86,896	19	<	<
31	C > T (U1102 only)	-	86,943	<	<	<
32	A > C (GS only)	N > K	86,949	<	<	<
33	G > T (U1102 only)	Q > K	87,011	<	<	<
34	T > C	K > R	87,016	22	<	<
35	A > G	-	87,036	21	<	<
36	C > T	A > T	87,092	16	<	<
37	C > T (U1102 and AJ)	R > H	87,100	16	<	<
38	A > G (GS only)	S > P	87,110	<	<	<

Table S1. Cont.

No.	SNPs U54 HHV-6A > CiHHV-6A	SNPs U54 Amino Acid	HHV-6A U1102	% HHV-6A Minor Variant SNPs in CiHHV-6A		
	HHV-6A:U1102, GS & AJ	Changes	Position	2284	5055	5814
39	C > A (GS only)	A > S	87,119	<	<	<
40	T > C (GS only)	M > V	87,128	<	<	<
41	G > C	N > K	87,129	20	<	<
42	G > A	H > Y	87,137	19	<	<
43	T > G	R > S	87,171	18	<	<
44	A > T	I > N	87,199	18	<	2
45	C > A	Q > R	87,204	18	<	<
46	T > C	Q > R	87,205	18	<	3
47	T > C	T > A	87,266	15	<	<
48	A > G	I > T	87,289	15	<	<
49	T > C (GS)	-	87,299	<	<	<
50	A > G (U1102 and AJ)	S > P	87,308	15	<	<
51	A > G (GS)	S > P	87,314	<	<	<

Mean read depths from new sequences from this study (methods 2.3) were for endogenous CiHHV-6A genomes from patients 2284, 5055 and 5814 it was 314, 9943 and 8941 respectively. Comparisons were made to all available reference genomes, from exogenous HHV-6A strains U1102, GS and AJ (methods 2.2). SNP% cutoffs were <0.5% reads indicated by <. Coding from the opposite strand. Brackets [] indicate same codon giving the coding change.

a. telomere - DR-L-----UL-----DR-R-sub-telomere-----//-----centromere
CiHHV-6A/B

b. DR: pac1-T1-DR1-DR6-T2-pac2

Figure S1. (a) Structure of CiHHV-6A/B underlined as integrated into the sub-telomeric region of human chromosomes. DR-L is the left direct repeat and DR-R is the right direct repeat in the prototype orientation of the virus genome, and bound the unique region, U, encoding most coding sequences; (b) The structure of the DR region from HHV-6A/B which includes the pac 1 and pac 2 DNA packaging signals, imperfect telomeric repeat region T1, perfect telomeric repeat region T2, and spliced coding sequences for genes DR1 and DR6. In the CiHHV-6A/B genomes the DR regions do not have the terminal pac sites.

Start of U41 Start ori-lyt (mori) 67610

HHV-6A.U1102 AACGGGAGCAGAAACTACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTTGATCACAGA 67641
GS AACGGGAGCAGAAACTACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTTGATCACAAA
AJ AACGGGAGCAGAAACTACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTTGATCACAAA
CiHHV-6A.5055 AACGGGAGCAGAAACTACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTTGATCACAAA
2284 AACGGGAGCAGAAACTACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTTGATCACAAA
5814 AACGGGAGCAGAAACTACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTTGATCACAAA
HHV-6B.Z29 AACAGGAGCAGAAACCACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTCGATCACAAA
HST AACAGGAGCAGAAACCACCGTTTCGTTTTTCATCAGCCATCTTTGTGGATTCGATCACAAA
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HHV-6A.U1102 AACAGAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC
GS AACAAAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC
AJ AACAAAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC
CiHHV-6A.5055 AACAAAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC
2284 AACAAAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC
5814 AACAAAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC
HHV-6B.Z29 AACAAAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC
HST AACAAAGATAATGGGGTTTTGTGGTGAATCCTTATATATATGTTTGACGTAACATAAC

HHV-6A.U1102 ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGAATTATACCGTTTTCTATATGAGGT
AJ ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGGATTATACCGTTTTCTATATGAGGT
GS ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGGATTATACCGTTTTCTATATGAGGT
CiHHV-6A.5055 ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGGATTATACCGTTTTCTATATGAGGT
2284 ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGGATTATACCGTTTTCTATATGAGGT
5814 ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGGATTATACCGTTTTCTATATGAGGT
HHV-6B.Z29 ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGAATATACCGTTTTCTATATGAGGT
HST ACGCGTCATCAAAACATAAGAGTAAACCACAAGTTGAATATACCGTTTTCTATATGAGGT

HHV-6A.U1102 TTACGGTCAAAGAAAAACGATTTTTTATGCAAATATTTCCACGCAGATGATATGACA
GS TTACGGCAAAAAGAAAAACGATTTTTTATGCAAATATTTCCACGCAGATGATATGACA
AJ TTACGGCAAAAAGAAAAACGATTTTTTATGCAAATATTTCCACGCAGATGATATGACA
CiHHV-6A.5055 TTACGGCAAAAAGAAAAACGATTTTTTATGCAAATATTTCCACGCAGATGATATGACA
2284 TTACGGCAAAAAGAAAAACGATTTTTTATGCAAAGATTTCCACGCAGATGATATGACA
5814 TTACGGCAAAAAGAAAAACGATTTTTTATGCAAAGATTTCCACGCAGATGATATGACA
HHV-6B.Z29 TTACGGCAAAAAGAAAAACGATTTTTCTTATGCAAATATTTCCACGCAGATGATATGACA
HST TTACGGCAAAAAGAAAAACGATTTTCTTATGCAAATATTTCCACGCAGATGATATGACA

OBP2

HHV-6A.U1102 CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA 67822
GS CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA
AJ CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA
CiHHV-6A.5055 CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA
2284 CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA
5814 CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA
HHV-6B.Z29 CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA
HST CGCCCTTAATTTAAATTTATGCAAATCGTCGTCACCTCAGGTACAATAGTATATTTATA

OBP1

HHV-6A.U1102 TATATATTTATTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA 67882
GS TATATATTTATTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA
AJ TATATATTTATTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA
CiHHV-6A.5055 TATATATTTATTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA
2284 TATATATTTATTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA
5814 TATATATTTATTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA
HHV-6B.Z29 TATATAGTTTTTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA
HST TATATAGTTTTTTAATAAACTTATTGAGGACGGGAGAACGAGGGCGTGGCGTTTACGTCA

HHV-6A.U1102 TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
GS TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
AJ TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
CiHHV-6A.5055 TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
2284 TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
5814 TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
HHV-6B.Z29 TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
HST TAGCCTAATTATGCATTTCTCAGAACAGGATTTAAAAGGCTGCGAGCGGCGGACTGTTCA
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HHV-6A.U1102 GAGGGACGCTGGGGTACGGCTTGATACGTTTGATTGAAAATGATTCCTCGTGCTATTTT
GS GAGGGACGCTGGGGTACGGCTTGAGACGTTTGATTGAAAATGATTCCTCGTGCTATTTT
AJ GAGGGACGCTGGGGTACGGCTTGAGACGTTTGATTGAAAATGATTCCTCGTGCTATTTT
CiHHV-6A.5055 GAGGGACGCTGGGGTACGGCTTGAGACGTTTGATTGAAAATGATTCCTCGTGCTATTTT
2284 GAGGGACGCTGGGGTACGGCTTGAGACGTTTGATTGAAAATGATTCCTCGTGCTATTTT
5814 GAGGGACGCTGGGGTACGGCTTGAGACGTTTGATTGAAAATGATTCCTCGTGCTATTTT

HHV-6B.Z29 GAGGGACGCTGGGGTACGACTTGAGACGTTTGACTGAAAAATGATCCTTCGTGTACTATTT
HST GAGGGACGCTGGGGTACGACTTGAGACGTTTGACTGAAAAATGATCCTTCGTGTACTATTT

HHV-6A.U1102 TCTGCAAAAAAATTAATTCGCCGGCGACAGTAAACTTTTCAGCGGAATTTCAAAAAATTA
GS TCTGCAAAAAAATTAATTCGCCGGCGACAGTAAACTTTTCAGCGGAATTTCAAAAAATTA
AJ TCTGCAAAAAAATTAATTCGCCGGCGACAGTAAACTTTTCAGCGGAATTTCAAAAAATTA
CiHHV-6A.5055 TCTGCAAAAAAATTAATTCGCCGGCGACAGTAAACTTTTCAGCGGAATTTCAAAAAATTA
2284 TCTGCAAAAAAATTAATTCGCCGGCGACAGTAAACTTTTCAGCGGAATTTCAAAAAATTA
5814 TCTGCAAAAAAATTAATTCGCCGGCGACAGTAAACTTTTCAGCGGAATTTCAAAAAATTA
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HST TCTACAAAAAATTAATTCGCCGGCGACAGTAAACTTTTCAGCGGAATTTCAAAAAATTA

I DR1

HHV-6.U1102 TTCCATATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG 68112
GS TTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG
AJ TTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG
CiHHV-6A.5055 TTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG
2284 TTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG
5814 TTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG
HHV-6B.Z29 TTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG
HST TTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGTAAAAACATATTTACG

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GS AATACAGTAGTTTTCGTGATATTTTTCGAAATTAATAAATTTTAAATCGGGTAAATGAT
AJ AATACAGTAGTTTTCGTGATATTTTTCGAAATTAATAAATTTTAAATCGGGTAAATGAT
CiHHV-6A.5055 AATACAGTAGTTTTCGTGATATTTTTCGAAATTAATAAATTTTAAATCGGGTAAATGAT
2284 AATACAGTAGTTTTCGTGATATTTTTCGAAATTAATAAATTTTAAATCGGGTAAATGAT
5814 AATACAGTAGTTTTCGTGATATTTTTCGAAATTAATAAATTTTAAATCGGGTAAATGAT
HHV-6B.Z29 AATACAGTAGTTTTCGTGATATTTTTCGAAATTAATAAATTTTAAATCGGGTAAATGAT
HST AATACAGTAGTTTTCGTGATATTTTTCGAAATTAATAAATTTTAAATCGGGTAAATGAT

U1102 indel-1

HHV-6.U1102 AAAGCATACTATTAGATTCCTCACGTTAACAAAGCAAGTTTTTTGAGGTTTTTCGGTATA 68242
GS AAAGCATACTA-----AGTTTTTT-GAGGTTTTTCGGTATA
AJ AAAGCATACTA-----AGTTTTTT-GAGGTTTTTCGGTATA
CiHHV-6A.5055 AAAGCATACTA-----AGTTTTTT-GAGGTTTTTCGGTATA
2284 AAAGCATACTATTAGATTCCTCACGTTAACAAAGCAAGTTTTTT GAGGTTTTTCGGTATA
5814 AAAGCATACTATTAGATTCCTCACGTTAACAAAGCAAGTTTTTT-GAGGTTTTTCGGTATA
HHV-6B.Z29 AAAGCATACTATTAGATTCCTCACGTTAACAGAGCAAGCTCTTC-GAGGTTTTTCAGTAGA
HST AAAGCATACTATTAGATTCCTCACGTTAACAGAGCAAGCTCTTC-GAGGTTTTTCAGTAGA

I DR2

HHV-6A.U1102 ATTTTAAACATTTACTTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGT 68302
GS ATGTTAAACATTTAGTTCCACATGTAATTTAAGCGTTTTAAAACGTATAGCTCACACGCGT
AJ ATGTTAAACATTTAGTTCCACATGTAATTTAAGCGTTTTAAAACGTATAGCTCACACGCGT
CiHHV-6A.5055 ATGTTAAACATTTAGTTCCACATGTAATTTAAGCGTTTTAAAACGTATAGCTCACACGCGT
2284 ATTTTAAACATTTAGTTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGT
5814 ATTTTAAACATTTAGTTCCACATGTAATTTAAGCATTTTAAAACGTATAACTCACACGCGT
HHV-6B.Z29 ATTTTCAATATTTA-----
HST ATTTTCAATATTTA-----

HHV-6A.U1102 AAAACATTTACGAATACAGTAGTTTTCGTGATATTTTTCGAAATTCAAAAAGTTTAAAT
GS AAAACATTTACGAATACAGTAGTTTTCGTGATATTTTTCGAAATTCAAAAATTTTAAAT
AJ AAAACATTTACGAATACAGTAGTTTTCGTGATATTTTTCGAAATTCAAAAATTTTAAAT
CiHHV-6A.5055 AAAACATTTACGAATACAGTAGTTTTCGTGATATTTTTCGAAATTCAAAAATTTTAAAT
2284 AAAACATTTACGAATACAGTAGTTTTCGTGATATTTTTCGAAATTCAAAAAGTTTAAAT
5814 AAAACATTTACGAATACAGTAGTTTTCGTGATATTTTTCGAAATTCAAAAAGTTTAAAT
HHV-6B.Z29 -----
HST -----

I DR3

HHV-6A.U1102 CGGGTAATGATAAAGCATATTTAGATTACACATGTAATTTAAGCATTTTAAAACGTA 68422
GS CGGGTAATGATAAAGCATATTTAGATTCCACATGTAATTTAAGCATTTTAAAACGTA
AJ CGGGTAATGATAAAGCATATTTAGATTCCACATGTAATTTAAGCATTTTAAAACGTA
CiHHV-6A.5055 CGGGTAATGATAAAGCATATTTAGATTCCACATGTAATTTAAGCATTTTAAAACGTA
2284 CGGGTAATGATAAAGCATATTTAGATTCCACATGTAATTTAAGCATTTTAAAACGTA
5814 CGGGTAATGATAAAGCATATTTAGATTACACATGTAATTTAAGCATTTTAAAACGTA
HHV-6B.Z29 -----ATTCCACATGTAATTTAAGCATTTTAAAATGTA
HST -----ATTCCACATGTAATTTAAGCATTTTAAAATGTA

HHV-6A.U1102 GAATTCACAAAGTGACAAAACATT--AAATACAGTAGTTTTCACGGTATTTTTCGAAAT
GS GAATTCACAAAGTGACAAAACATTCACAAATACAGTAGTTTTCACGGTATTTTTCGGGAT
AJ GAATTCACAAAGTGACAAAACATTCACAAATACAGTAGTTTTCACGGTATTTTTCGGGAT
CiHHV-6A.5055 GAATTCACAAAGTGACAAAACATTCACAAATACAGTAGTTTTCACGGTATTTTTCGGGAT

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2284      GAATTCACAAAGTGACAAAACATTGACGAATACAGTAGTTTTTCACGGTATTTTTTGAAT
5814      GAATTCACAAAGTGACAAAACATTGACGAATACAGTAGTTTTTCACGGTATTTTTTGAAT
HHV-6B.Z29  GAATTCACAAAGTGACAAAACATTGACGAATACAGTAGTTTTTCACGGTATTTTTT-GAAAT
HST      GAATTCACAAAGTGACAAAACATTGACGAATACAGTAGTTTTTCACGGTATTTTTT-GAAAT
*****

HHV-6A.U1102  TAA---ATTTTAAATCGGGTACATGATAAAGCATGCTGTTAAATTCACGTTTTTAGGGCA
GS      TAA---ATTTTAAATCGGGTAAATGACAAAGCATGCTGTTAAATTCACGTTTTTAGGGCA
AJ      TAA---ATTTTAAATCGGGTAAATGACAAAGCATGCTGTTAAATTCACGTTTTTAGGGCA
CiHHV-6A.5055  TAA---ATTTTAAATCGGGTAAATGACAAAGCATGCTGTTAAATTCACGTTTTTAGGGCA
2284      TAA---ATTTTAAATCGGGTAAATGATAAAGCATGCTGTTAAATTCACATTTTTTAGGGCA
5814      TAA---ATTTTAAATCGGGTAAATGATAAAGCATGCTGTTAAATTCACATTTTTTAGGGCA
HHV-6B.Z29  TAATAAATTTTAAATCGGGTAAATGGTAAAGCATGCTGTTAAATTCACGTTAACACAGAGCA
HST      TAATAAATTTTAAATCGGGTAAATGGTAAAGCATGCTGTTAAATTCACGTTAAAGAGAGCA
*****

HHV-6A.U1102  AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAATGTATTCAGCGTTTCAATTTTAGAT
GS      AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAAT--ATTCAGCGTTTCAATTTTAGAT
AJ      AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAAT--ATTCAGCGTTTCAATTTTAGAT
CiHHV-6A.5055  AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAAT--ATTCAGCGTTTCAATTTTAGAT
2284      AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAATGTATTCAGCGTTTCAATTTTAGAT
5814      AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAATGTATTCAGCGTTTCAATTTTAGAT
HHV-6B.Z29  AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAATGTATTTAGTATTTCAATTTTAGAT
HST      AGTTCGCGAGGTTTGCTCTGTGATTATCAGTGAATGTATTTAGTATTTCAATTTTAGAT
*****

                               U1102 indel-2      End ori-lyt (mori) 68712
HHV-6A.U1102  TATGGTTCGGTAAAAATATAGGTCCTTGTAATCATTGATTAGCTTTTATATGTATT 68714
GS      TATGGTTCGGTAAAAATATAGGTCCTTG-----
AJ      TATGGTTCGGTAAAAATATAGGTCCTTG-----
CiHHV-6A.5055  TATGGTTCGGTAAAAATATAGGTCCTTG-----
2284      TATGGTTCGGTAAAAATATAGGTCCTTGTAAATCATTGATTAGCTTTTATATGTATT
5814      TATGGTTCGGTAAAAATATAGGTCCTTGTAAATCATTGATTAGCTTTTATATGTATT
HHV-6B.Z29  CATGGTTCGGTAAAGATATAAGTCCGTGTAATAATTTTTGGTTTAGTTTTCATATCTACT
HST      CATGGTTCGGTAAAGATATAAGTCCGTGTAATAATTTTTGGTTTAGTTTTCATATCTACT
*****

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Figure S2. The origin of lytic replication, *mori*, of CiHHV-6A 5055/1623, 5814, and 2284/4305 compared to virus reference HHV-6A U1102, AJ, GS and HHV-6B Z29, HST.

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