Supporting Information

A herpesvirus transactivator and cellular POU proteins extensively regulate DNA binding of the host Notch signaling protein RBP-Jk to the virus genome

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Contents:

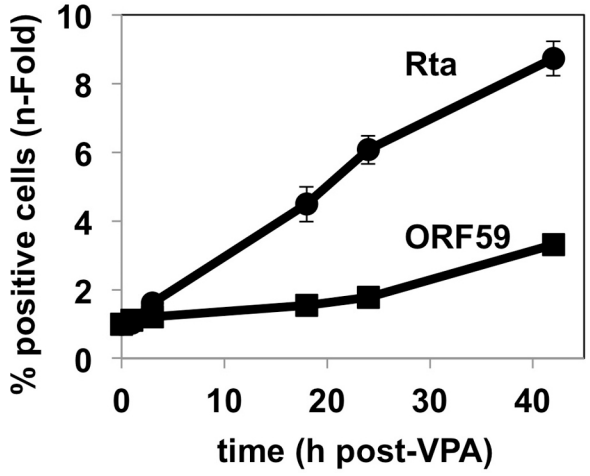

Figure S1. Kinetics of Rta and DE gene expression in VPA-treated BC-3 cells. Duplicate cultures of BC-3 cells were either left untreated or treated with 1mM VPA. At the indicated timepoints, cells were harvested and $2.5x10^5$ cells/200µl were adhered to poly-*L*-lysine (Sigma)-coated glasses slides in circles drawn with a Pap pen (Life Technologies) for 30 minutes at room temperature. Cells were fixed by incubation in pre-chilled methanol: acetone (1:1), -20°C for 10 minutes. After fixation, cells were blocked using fresh 3% BSA/1% glycine in 1xPBS at room temperature for 30 minutes. Proteins were detected by indirect immunofluorescence using primary rabbit anti-Rta and mouse anti-ORF59 (Santa Cruz Biotechnology; 1:1000 in blocking buffer) at room temperature for 1 hour, followed by two washes in 1xPBS 0.4% Tween 20 for 30 minutes, then one wash in 1xPBS for 30 minutes. Secondary antibodies were goat anti-rabbit Dylight 488 Conjugated (Invitrogen) and goat anti-Mouse Dylight 550 conjugated (Thermo Scientific;1:500 in blocking buffer) at room temperature for 1 hour, followed by washes as described above. Cover slips were mounted inverted in Vectashield (Vector Labs). Reactivation was scored by counting >1500 cells, then dividing the number of cells expressing Rta, or ORF59, by the total number of cells in >10 fields per replicate, for each circle, to determine percent reactivation. Fold reactivation was determined by dividing percent of antigen expressing cells at each time point by percent at time 0 (untreated) and plotted above.

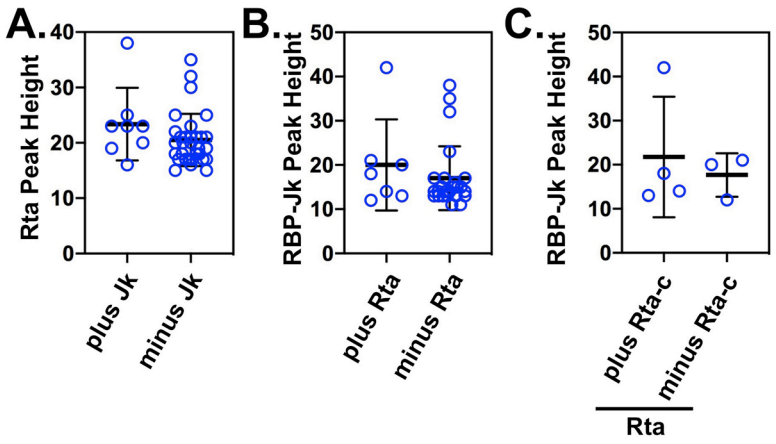

Figure S2. The median heights of Rta and RBP-Jk peaks associated with each other and Rta-c motifs. Peak height ranges (read depth/bp) for the indicated groups of peaks in viral DE promoters. Thick lines show Median heights, thin lines show boundaries of 2nd and third quartiles. **(A)** Rta peak heights. "Jk"=RBP-Jk **(B and C).** RBP-Jk peak heights.

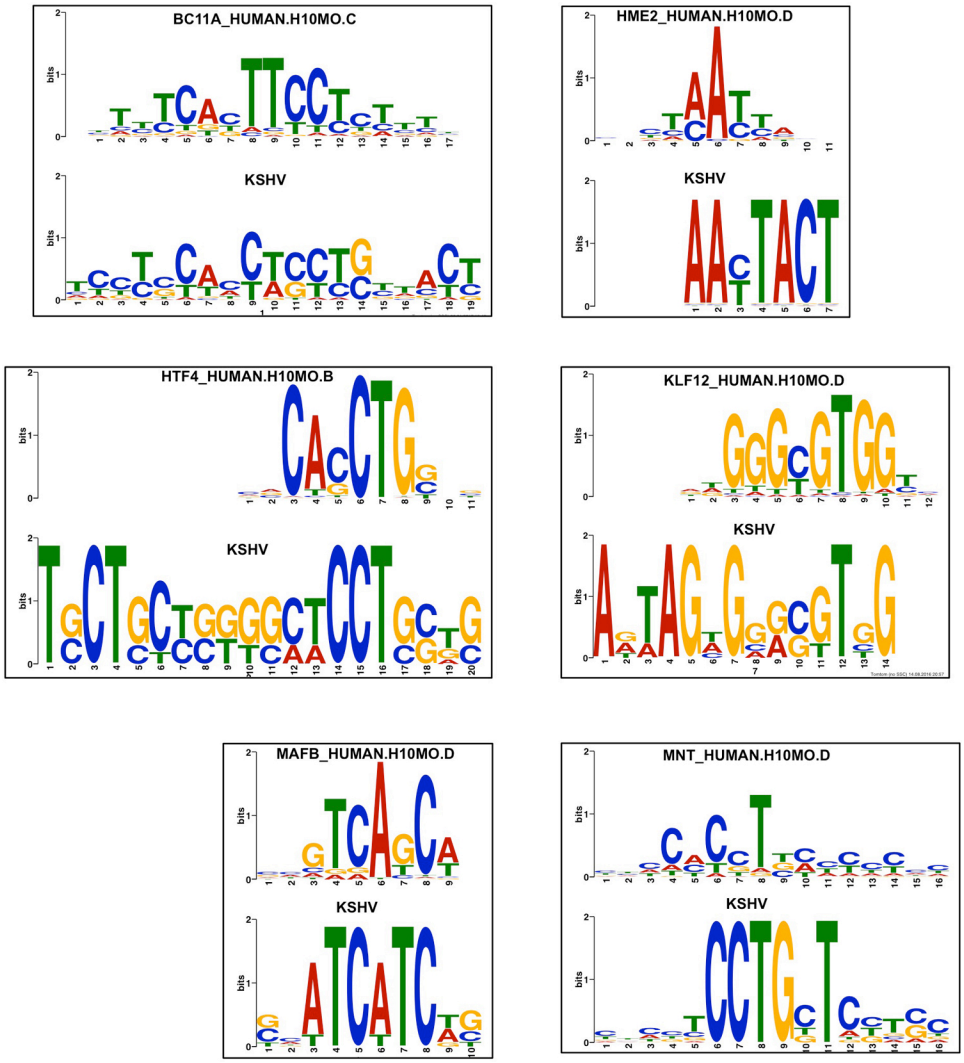

Figure S3. Sequence logos for DNA motifs associated preferentially with RBP-Jk Class 2 peaks. Motifs were identified using a discriminative MEME search described in Table 3 (40). The KSHV genome was searched for occurrences of matches to each consensus motif in the KSHV genome using the FIMO algorithm (117). Sequence logos were generated for the resulting set of matching motifs.

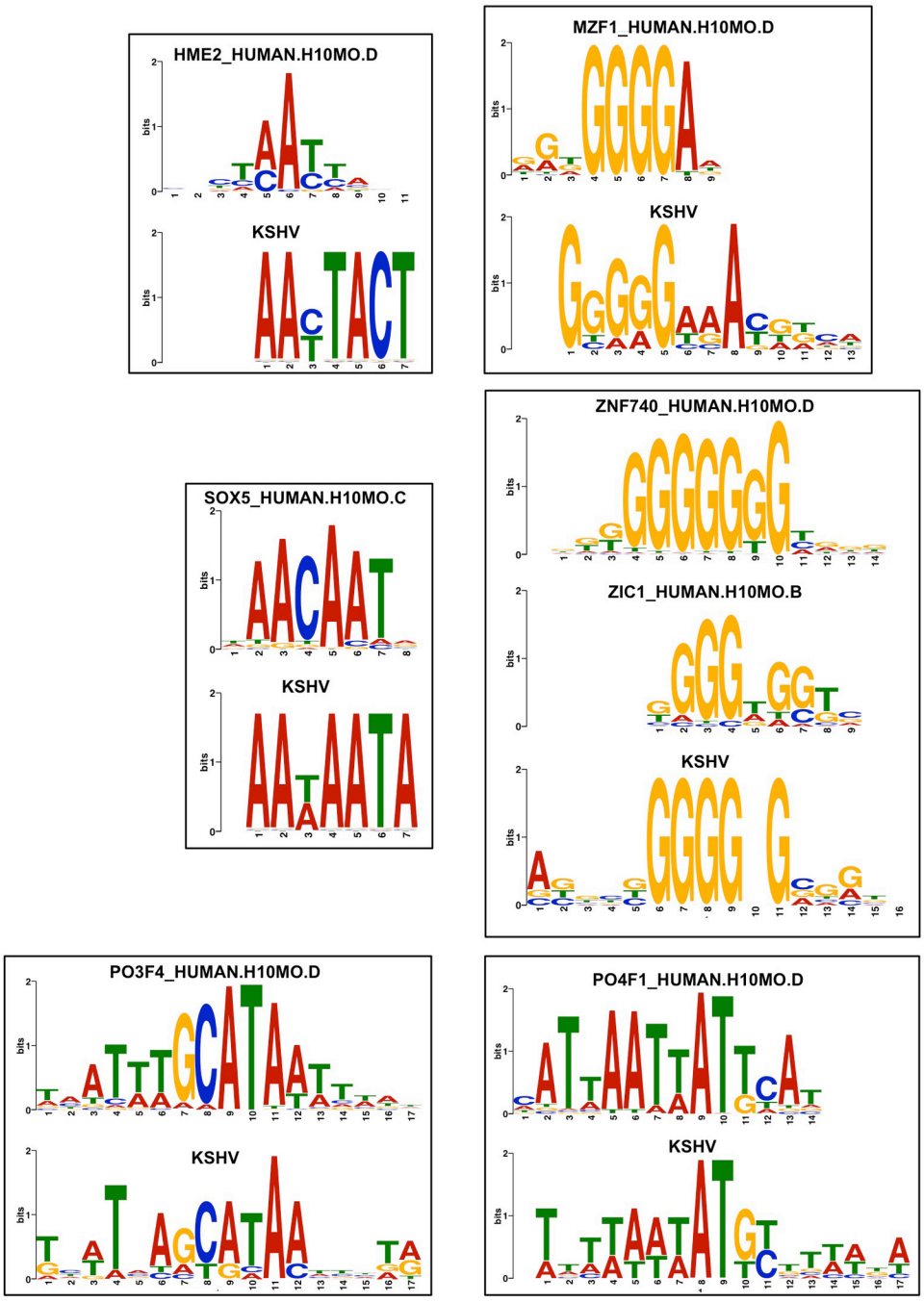

Figure S4. Sequence logos for DNA motifs associated preferentially with RBP-Jk Class 2/Rta peaks. Motifs were identified using a discriminative MEME search described in Table 4 (40). The KSHV genome was searched for occurrences of matches to each consensus motif in the KSHV genome using the FIMO algorithm (117). Sequence logos were generated for the resulting set of matching motifs.

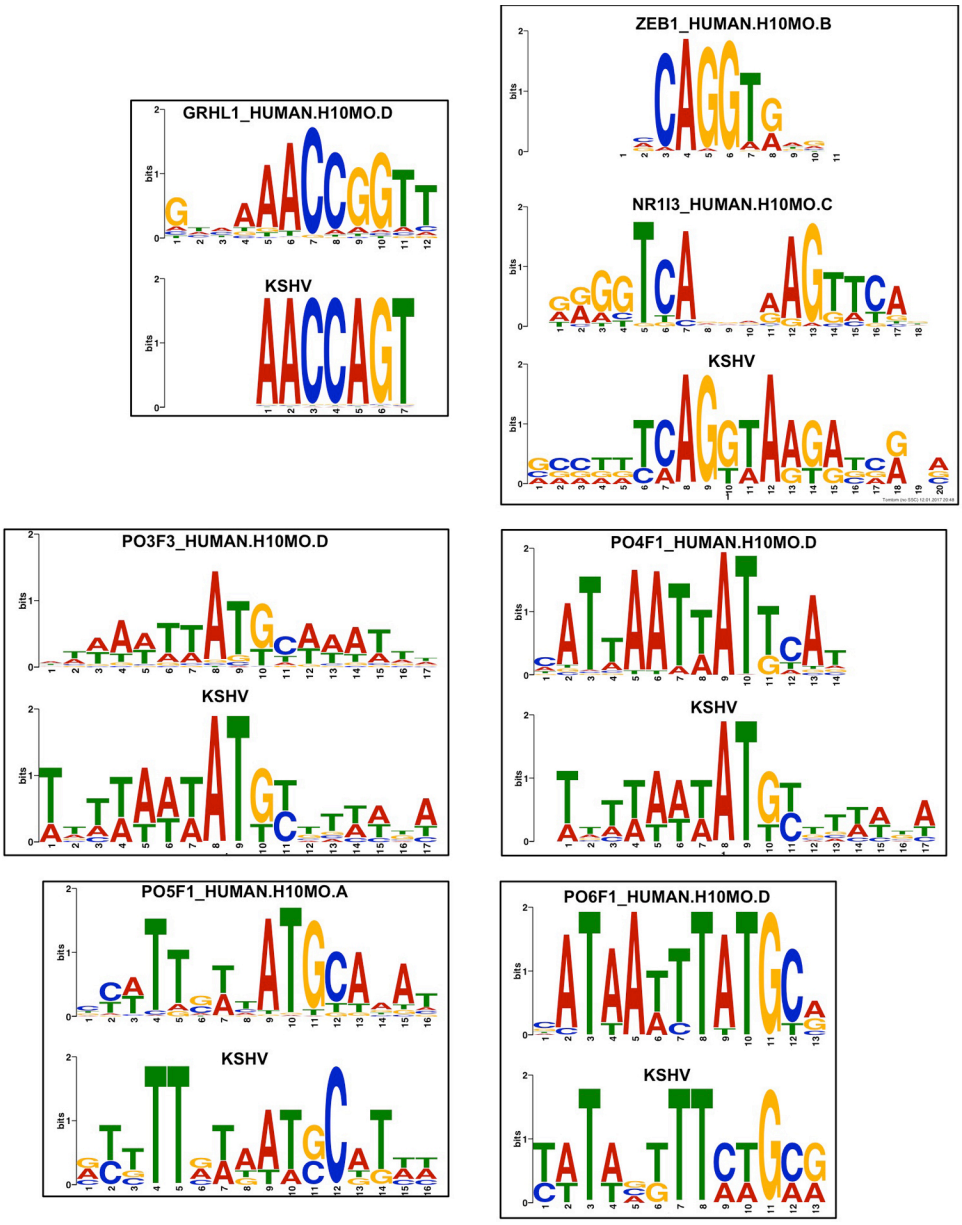

Figure S5. Sequence logos for DNA motifs associated preferentially with RBP-Jk Class 5 peaks. Motifs were identified using a discriminative MEME search described in Table 5 (40). The KSHV genome was searched for occurrences of matches to each consensus motif in the KSHV genome using the FIMO algorithm (117). Sequence logos were generated for the resulting set of matching motifs.

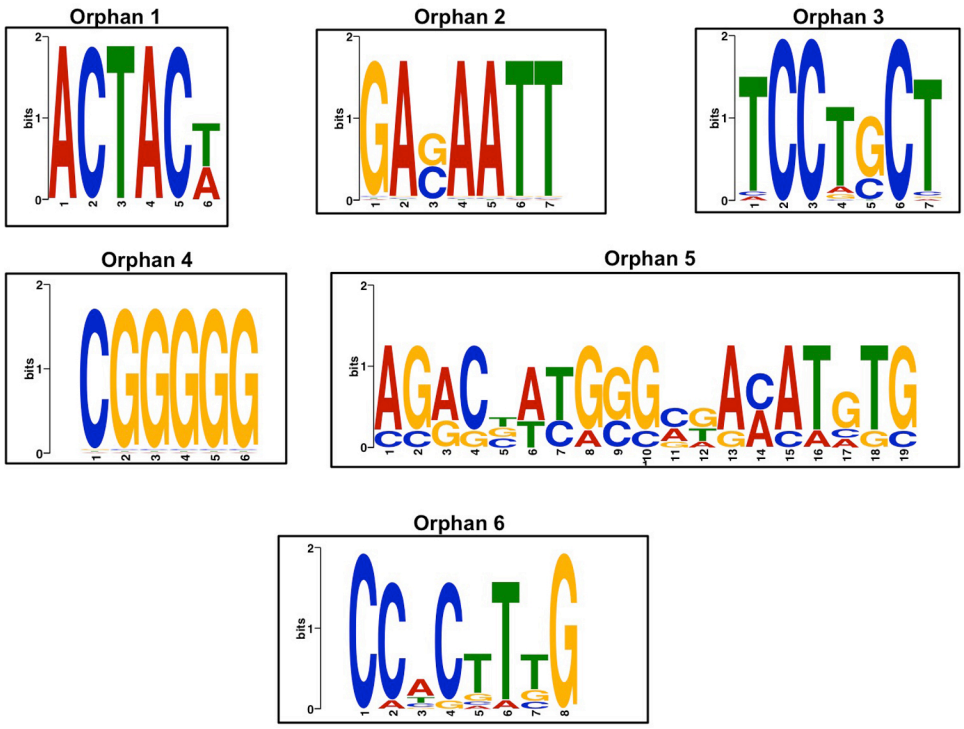

Figure S6. Sequence logos for orphan motifs. Motifs were identified using a discriminative MEME search described in Table S3 (40). The KSHV genome was searched for occurrences of matches to each consensus motif in the KSHV genome using the FIMO algorithm (117). Sequence logos were generated for the resulting set of matching motifs.

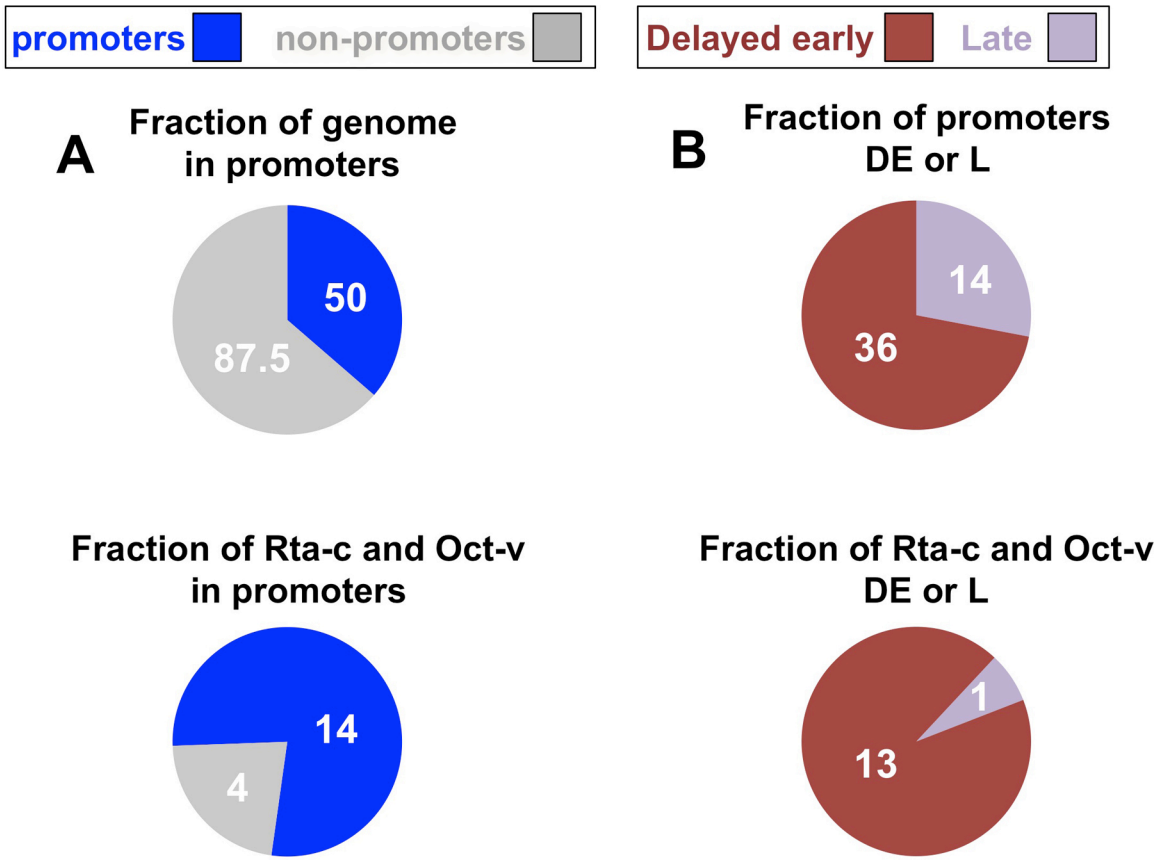

Figure S7. Coincident Rta-c/Oct-v motifs are overrepresented in KSHV DE promoters.
(A) Proportion of Rta-c/Oct-v motifs in promoters. Blue segments represent proportion of KSHV genome located in promoters. Grey segments represent proportion of genome outside of promoters. Numbers indicate kb. of sequence at top, number of Rta-c/Oct-v motifs at bottom. **(B) Proportion of Rta-c/Oct-v motifs in delayed early vs. late promoters.** Brown segments represent proportion of genome in KSHV DE promoters. Purple segments represent proportion of KSHV L promoters. Numbers indicate numbers of promoters at top, and number of Rta-c/Oct-v motifs at bottom.

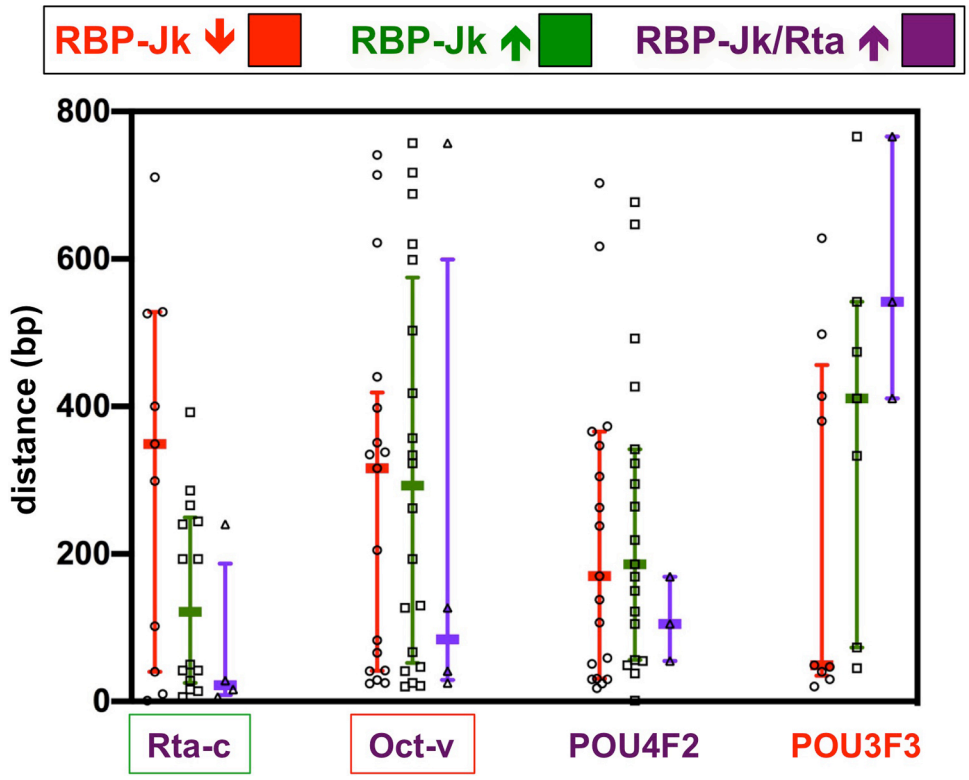

Figure S8. Rta-c and Oct-v motifs are closer to Jk2 peaks than to Jk5 peaks. The range of shortest distances between each RBP-Jk peak and each of the motifs indicated on the x axis was calculated in all viral DE promoter DNA. Thick lines show median heights, thin lines show boundaries of 2nd and third quartiles.

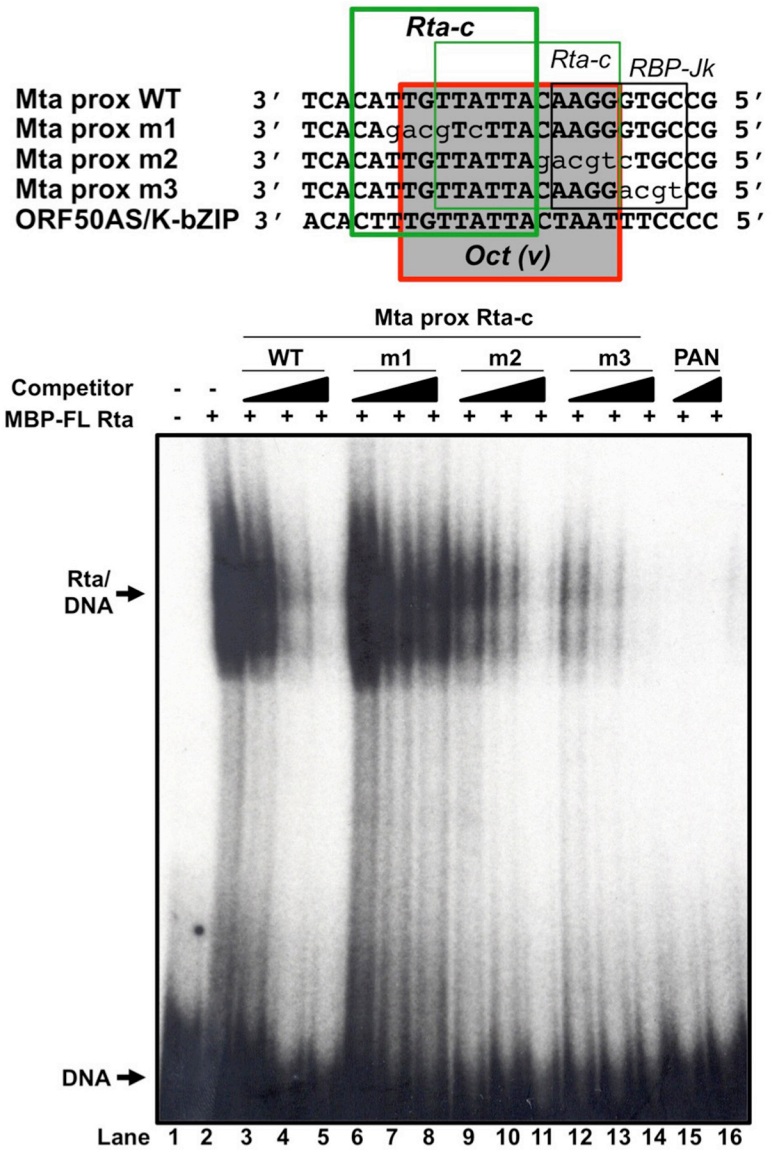

Figure S9. Rta binds sequence-specifically to the Rta-c/Oct-v motif from the ORF50AS/K-bZIP promoter. Increasing amounts of the indicated, un-labeled competitor DNAs were pre-incubated with MBP FL-Rta, before addition of ^{32}P-labeled ORF50AS/K-bZIP DNA. Mixtures were electrophoresed and visualized by autoradiography. Sequences of the oligos are shown at the top. The motifs conserved in the Mta and ORF50AS/K-bZIP promoters are labeled in bold; standard labels show the motifs found only in Mta.

Table S1. Genome wide analysis of Rta and RBP-Jk DNA binding on the KSHV genome during latency and reactivation: data. (A). Rta (+VPA) **(B)**. RBP-Jk (+VPA) **(C)**. RBP-Jk (-VPA) **(D)**. Rta and RBP-Jk (+VPA) co-localized peaks. Abbreviations: Chr=chromosome input for MACS2 read mapping, start=genome position of start of peak (bp), end=genome position of end of peak (bp), length=length of peak (bp), abs_summit=peak summit, pileup=height in read depth of peak summit, Kinetics= Replication kinetics of transcription start sites corresponding to promoters (DE=delayed early, L=Late)), Rank by height=rank of individual peak heights in descending order. On Table D, green text=RBP-Jk peak increased in reactivation, red text=RBP-Jk peak decreased in reactivation.

Table S1A. Rta (+VPA) peaks

Peak #	chr	start	end	length	abs_summit	pileup	Promoter	Kinetics	Rank by Height
1	gi|2065526|gb|U75698.1|KSU75698	786	1352	567	875	35	ORF4	DE	5
2	gi|2065526|gb|U75698.1|KSU75698	1427	1646	220	1568	22			22
3	gi|2065526|gb|U75698.1|KSU75698	1705	2483	779	1881	25			10
4	gi|2065526|gb|U75698.1|KSU75698	2530	2629	100	2539	16	ORF6	DE	93
5	gi|2065526|gb|U75698.1|KSU75698	2663	2993	331	2716	18	ORF6	DE	63
6	gi|2065526|gb|U75698.1|KSU75698	3754	3922	169	3849	16			94
7	gi|2065526|gb|U75698.1|KSU75698	4581	4716	136	4602	17			75
8	gi|2065526|gb|U75698.1|KSU75698	4884	4993	110	4910	18			64
9	gi|2065526|gb|U75698.1|KSU75698	6070	6293	224	6158	16			95
10	gi|2065526|gb|U75698.1|KSU75698	6612	6819	208	6759	17			76
11	gi|2065526|gb|U75698.1|KSU75698	7495	7658	164	7519	17			77
12	gi|2065526|gb|U75698.1|KSU75698	12465	12730	266	12548	17			78
13	gi|2065526|gb|U75698.1|KSU75698	15956	16055	100	15986	19			48
14	gi|2065526|gb|U75698.1|KSU75698	17172	17271	100	17185	16			96
15	gi|2065526|gb|U75698.1|KSU75698	18218	18409	192	18302	17	vIL6	DE	79
16	gi|2065526|gb|U75698.1|KSU75698	19126	19264	139	19190	20			33
17	gi|2065526|gb|U75698.1|KSU75698	19940	20079	140	19968	15	K3int	DE	102
18	gi|2065526|gb|U75698.1|KSU75698	22694	22832	139	22768	25	K4	DE	11
19	gi|2065526|gb|U75698.1|KSU75698	22943	23188	246	23096	32	K4.1/4.2	DE	6
20	gi|2065526|gb|U75698.1|KSU75698	24173	24605	433	24425	41			3
21	gi|2065526|gb|U75698.1|KSU75698	28288	28421	134	28355	23	K6/K6.2/PAN	DE/DE/DE	16
22	gi|2065526|gb|U75698.1|KSU75698	28472	28808	337	28617	30	K6/PAN	DE/DE	8
23	gi|2065526|gb|U75698.1|KSU75698	29508	29607	100	29574	16	ORF16	DE	97
24	gi|2065526|gb|U75698.1|KSU75698	29706	29811	106	29788	20	ORF16	DE	34
25	gi|2065526|gb|U75698.1|KSU75698	30071	30170	100	30125	17			80
26	gi|2065526|gb|U75698.1|KSU75698	33105	33204	100	33184	18	ORF17	L	65
27	gi|2065526|gb|U75698.1|KSU75698	34605	34716	112	34628	15	ORF21	L	103
28	gi|2065526|gb|U75698.1|KSU75698	37032	37131	100	37116	18			66
29	gi|2065526|gb|U75698.1|KSU75698	39207	39306	100	39281	17			81
30	gi|2065526|gb|U75698.1|KSU75698	39540	39705	166	39611	20			35
31	gi|2065526|gb|U75698.1|KSU75698	42083	42327	245	42252	21	ORF25	L	23
32	gi|2065526|gb|U75698.1|KSU75698	44138	44339	202	44221	20			36
33	gi|2065526|gb|U75698.1|KSU75698	45271	45452	182	45357	20			37
34	gi|2065526|gb|U75698.1|KSU75698	45880	46028	149	45953	23	ORF26	L	17
35	gi|2065526|gb|U75698.1|KSU75698	46867	47026	160	46951	17	ORF27	L	82
36	gi|2065526|gb|U75698.1|KSU75698	51506	51834	329	51546	18			67
37	gi|2065526|gb|U75698.1|KSU75698	52641	52745	105	52660	17	ORF33	L	83
38	gi|2065526|gb|U75698.1|KSU75698	52806	53024	219	52929	20			38
39	gi|2065526|gb|U75698.1|KSU75698	54848	54984	137	54896	17	ORF35	DE	84
40	gi|2065526|gb|U75698.1|KSU75698	55379	55521	143	55460	21	ORF35	DE	24
41	gi|2065526|gb|U75698.1|KSU75698	55670	55840	171	55786	20			39
42	gi|2065526|gb|U75698.1|KSU75698	59287	59397	111	59368	18			68
43	gi|2065526|gb|U75698.1|KSU75698	59607	59707	101	59698	19			49
44	gi|2065526|gb|U75698.1|KSU75698	61238	61364	127	61281	17			85
45	gi|2065526|gb|U75698.1|KSU75698	63287	63404	118	63341	19			50
46	gi|2065526|gb|U75698.1|KSU75698	66392	66500	109	66457	19			51
47	gi|2065526|gb|U75698.1|KSU75698	66774	66912	139	66899	16			98
48	gi|2065526|gb|U75698.1|KSU75698	68562	68665	104	68602	15			104
49	gi|2065526|gb|U75698.1|KSU75698	68973	69253	281	69005	19	ORF45/50	DE/DE	52
50	gi|2065526|gb|U75698.1|KSU75698	69560	69713	154	69618	18	ORF45/45.1/50	DE/DE/DE	69
51	gi|2065526|gb|U75698.1|KSU75698	70022	70121	100	70086	19	ORF45.1/46-47/50	DE/DE/DE	53
52	gi|2065526|gb|U75698.1|KSU75698	70163	70509	347	70284	25	ORF46-47/50	DE/DE	12
53	gi|2065526|gb|U75698.1|KSU75698	70664	71086	423	71004	23	ORF50	DE	18
54	gi|2065526|gb|U75698.1|KSU75698	71279	71484	206	71410	23	ORF50	DE	19
55	gi|2065526|gb|U75698.1|KSU75698	72523	73198	676	72909	30			9
56	gi|2065526|gb|U75698.1|KSU75698	73276	74056	781	73655	25			13
57	gi|2065526|gb|U75698.1|KSU75698	74177	74971	795	74720	38	ORF50AS/KbZIP	DE	4
58	gi|2065526|gb|U75698.1|KSU75698	75100	75328	229	75151	20	ORF50AS/K8.1	DE/L	40
59	gi|2065526|gb|U75698.1|KSU75698	75748	75858	111	75823	17	K8.1	L	86
60	gi|2065526|gb|U75698.1|KSU75698	77312	77455	144	77382	17	ORF52	DE	87
61	gi|2065526|gb|U75698.1|KSU75698	77889	78040	152	77958	20	ORF52/53	DE/DE	41
62	gi|2065526|gb|U75698.1|KSU75698	78160	78281	122	78244	21	ORF53	DE	25
63	gi|2065526|gb|U75698.1|KSU75698	81220	81361	142	81306	21	ORF57	DE	26
64	gi|2065526|gb|U75698.1|KSU75698	81820	81959	140	81901	16	ORF57	DE	99
65	gi|2065526|gb|U75698.1|KSU75698	83031	83162	132	83091	19			54
66	gi|2065526|gb|U75698.1|KSU75698	86214	86366	153	86295	21			27

67	gi|2065526|gb|U75698.1|KSU75698	88621	88787	167	88745	21			28
68	gi|2065526|gb|U75698.1|KSU75698	89809	89945	137	89892	20			42
69	gi|2065526|gb|U75698.1|KSU75698	92629	93000	372	92700	25			14
70	gi|2065526|gb|U75698.1|KSU75698	94514	94636	123	94552	19			55
71	gi|2065526|gb|U75698.1|KSU75698	95078	95229	152	95171	21			29
72	gi|2065526|gb|U75698.1|KSU75698	96712	96945	234	96880	20	ORF58-59	DE	43
73	gi|2065526|gb|U75698.1|KSU75698	97841	97993	153	97911	20			44
74	gi|2065526|gb|U75698.1|KSU75698	98148	98278	131	98217	17			88
75	gi|2065526|gb|U75698.1|KSU75698	98447	98711	265	98497	20			45
76	gi|2065526|gb|U75698.1|KSU75698	99176	99279	104	99227	17			89
77	gi|2065526|gb|U75698.1|KSU75698	100415	100518	104	100438	21	ORF60-61	DE	30
78	gi|2065526|gb|U75698.1|KSU75698	102701	102880	180	102841	16			100
79	gi|2065526|gb|U75698.1|KSU75698	103072	103205	134	103113	18			70
80	gi|2065526|gb|U75698.1|KSU75698	104391	104651	261	104568	19			56
81	gi|2065526|gb|U75698.1|KSU75698	105302	105427	126	105342	19			57
82	gi|2065526|gb|U75698.1|KSU75698	105668	105814	147	105735	23			20
83	gi|2065526|gb|U75698.1|KSU75698	106325	106445	121	106407	19			58
84	gi|2065526|gb|U75698.1|KSU75698	106554	106692	139	106642	19			59
85	gi|2065526|gb|U75698.1|KSU75698	106938	107190	253	107125	21			31
86	gi|2065526|gb|U75698.1|KSU75698	110254	110423	170	110342	16			101
87	gi|2065526|gb|U75698.1|KSU75698	110575	110774	200	110685	19			60
88	gi|2065526|gb|U75698.1|KSU75698	112362	112539	178	112483	18			71
89	gi|2065526|gb|U75698.1|KSU75698	113706	113822	117	113773	17			90
90	gi|2065526|gb|U75698.1|KSU75698	118038	118425	388	118176	31			7
91	gi|2065526|gb|U75698.1|KSU75698	118694	118921	228	118859	20	K12	L	46
92	gi|2065526|gb|U75698.1|KSU75698	119099	119200	102	119190	19	K12	L	61
93	gi|2065526|gb|U75698.1|KSU75698	120035	120373	339	120187	24			15
94	gi|2065526|gb|U75698.1|KSU75698	120628	120729	102	120690	23			21
95	gi|2065526|gb|U75698.1|KSU75698	121205	121320	116	121302	18			72
96	gi|2065526|gb|U75698.1|KSU75698	122306	122479	174	122356	17			91
97	gi|2065526|gb|U75698.1|KSU75698	122649	122749	101	122715	18			73
98	gi|2065526|gb|U75698.1|KSU75698	124778	125107	330	124873	44			2
99	gi|2065526|gb|U75698.1|KSU75698	125235	125341	107	125291	20			47
100	gi|2065526|gb|U75698.1|KSU75698	125427	126467	1041	125758	45			1
101	gi|2065526|gb|U75698.1|KSU75698	126940	127059	120	126993	21	K14/ORF74	DE/DE	32
102	gi|2065526|gb|U75698.1|KSU75698	128286	128403	118	128326	18	ORF73	DE	74
103	gi|2065526|gb|U75698.1|KSU75698	130893	131005	113	130919	17			92
104	gi|2065526|gb|U75698.1|KSU75698	133717	133840	124	133776	19			62

Table S1B. RBP-Jk (+VPA) peaks

Peak #	chr	start	end	length	abs_summit	pileup	Promoter	Kinetics	Rank by Height
1	gi|2065526|gb|U75698.1|KSU75698	1583	1751	169	1687	12			77
2	gi|2065526|gb|U75698.1|KSU75698	2263	2447	185	2295	13	ORF6	DE	56
3	gi|2065526|gb|U75698.1|KSU75698	2643	2842	200	2704	12	ORF6	DE	78
4	gi|2065526|gb|U75698.1|KSU75698	4424	4561	138	4508	14			40
5	gi|2065526|gb|U75698.1|KSU75698	4772	4912	141	4837	14			41
6	gi|2065526|gb|U75698.1|KSU75698	6088	6406	319	6139	16			26
7	gi|2065526|gb|U75698.1|KSU75698	6088	6406	319	6346	13			57
8	gi|2065526|gb|U75698.1|KSU75698	8223	8327	105	8294	15	ORF8	DE	30
9	gi|2065526|gb|U75698.1|KSU75698	8422	8536	115	8471	17	ORF8	DE	20
10	gi|2065526|gb|U75698.1|KSU75698	11504	11686	183	11553	14			42
11	gi|2065526|gb|U75698.1|KSU75698	15486	15592	107	15540	17	ORF11	DE	21
12	gi|2065526|gb|U75698.1|KSU75698	18683	18830	148	18756	14	vIL6	DE	43
13	gi|2065526|gb|U75698.1|KSU75698	19212	19311	100	19267	14	K3-int	DE	44
14	gi|2065526|gb|U75698.1|KSU75698	24265	24604	340	24350	22			13
15	gi|2065526|gb|U75698.1|KSU75698	24265	24604	340	24521	23			11
16	gi|2065526|gb|U75698.1|KSU75698	25316	25521	206	25400	14			45
17	gi|2065526|gb|U75698.1|KSU75698	27765	27962	198	27853	13	K6/K6.2/K7/PAN	DE/DE/DE/DE	58
18	gi|2065526|gb|U75698.1|KSU75698	29929	30142	214	30107	15			31
19	gi|2065526|gb|U75698.1|KSU75698	31367	31466	100	31443	13			59
20	gi|2065526|gb|U75698.1|KSU75698	36434	36533	100	36446	11			84
21	gi|2065526|gb|U75698.1|KSU75698	38120	38219	100	38156	11			85
22	gi|2065526|gb|U75698.1|KSU75698	39309	39483	175	39406	13			60
23	gi|2065526|gb|U75698.1|KSU75698	39581	39685	105	39634	15			32
24	gi|2065526|gb|U75698.1|KSU75698	39837	39959	123	39906	16			27
25	gi|2065526|gb|U75698.1|KSU75698	40770	40873	104	40816	13			61
26	gi|2065526|gb|U75698.1|KSU75698	43819	43922	104	43867	17			22
27	gi|2065526|gb|U75698.1|KSU75698	48122	48221	100	48127	13	ORF28	L	62
28	gi|2065526|gb|U75698.1|KSU75698	50520	50683	164	50655	14			46
29	gi|2065526|gb|U75698.1|KSU75698	52774	52876	103	52812	11			86
30	gi|2065526|gb|U75698.1|KSU75698	53682	53798	117	53756	13	ORF34	DE	63
31	gi|2065526|gb|U75698.1|KSU75698	53918	54058	141	53999	15	ORF34	DE	33
32	gi|2065526|gb|U75698.1|KSU75698	56276	56440	165	56375	15			34
33	gi|2065526|gb|U75698.1|KSU75698	57531	57701	171	57561	11	ORF38	DE	87
34	gi|2065526|gb|U75698.1|KSU75698	59266	59377	112	59305	12			79
35	gi|2065526|gb|U75698.1|KSU75698	65484	65583	100	65531	15			35
36	gi|2065526|gb|U75698.1|KSU75698	66116	66230	115	66173	15			36
37	gi|2065526|gb|U75698.1|KSU75698	67261	67417	157	67340	14			47
38	gi|2065526|gb|U75698.1|KSU75698	69778	70442	665	69850	14	ORF45/45.1/50	DE/DE/DE	48
39	gi|2065526|gb|U75698.1|KSU75698	69778	70442	665	70059	18	ORF45.1/46-47/50	DE/DE/DE	17
40	gi|2065526|gb|U75698.1|KSU75698	69778	70442	665	70283	20	ORF46-47/50	DE/DE	16
41	gi|2065526|gb|U75698.1|KSU75698	70531	70630	100	70615	13	ORF46-47/50	DE/DE	64
42	gi|2065526|gb|U75698.1|KSU75698	70944	71079	136	71015	14	ORF50	DE	49
43	gi|2065526|gb|U75698.1|KSU75698	71212	71657	446	71287	14	ORF50	DE	50
44	gi|2065526|gb|U75698.1|KSU75698	71212	71657	446	71435	21	ORF50	DE	14
45	gi|2065526|gb|U75698.1|KSU75698	71212	71657	446	71575	17			23
46	gi|2065526|gb|U75698.1|KSU75698	71726	71916	191	71779	13			65
47	gi|2065526|gb|U75698.1|KSU75698	72576	73200	625	72642	15			37
48	gi|2065526|gb|U75698.1|KSU75698	72576	73200	625	73128	17			24
49	gi|2065526|gb|U75698.1|KSU75698	73390	73489	100	73423	12			80
50	gi|2065526|gb|U75698.1|KSU75698	73996	74878	883	74098	35	KbZIP	DE	4
51	gi|2065526|gb|U75698.1|KSU75698	73996	74878	883	74283	32	KbZIP	DE	5
52	gi|2065526|gb|U75698.1|KSU75698	73996	74878	883	74452	38	KbZIP	DE	3
53	gi|2065526|gb|U75698.1|KSU75698	73996	74878	883	74719	42	ORF50AS/KbZIP	DE	1
54	gi|2065526|gb|U75698.1|KSU75698	75155	75264	110	75204	14	ORF50AS/K8.1	DE/L	51
55	gi|2065526|gb|U75698.1|KSU75698	78802	78914	113	78858	13	ORF55	DE	66
56	gi|2065526|gb|U75698.1|KSU75698	81510	81760	251	81596	16	ORF57	DE	28
57	gi|2065526|gb|U75698.1|KSU75698	81828	81973	146	81962	13	ORF57	DE	67
58	gi|2065526|gb|U75698.1|KSU75698	83540	83682	143	83612	21			15
59	gi|2065526|gb|U75698.1|KSU75698	86125	86309	185	86184	11			88
60	gi|2065526|gb|U75698.1|KSU75698	88430	88617	188	88484	12			81
61	gi|2065526|gb|U75698.1|KSU75698	90892	91045	154	90936	13			68
62	gi|2065526|gb|U75698.1|KSU75698	92715	92814	100	92760	13			69
63	gi|2065526|gb|U75698.1|KSU75698	92899	93225	327	92948	13			70
64	gi|2065526|gb|U75698.1|KSU75698	92899	93225	327	93068	13			71
65	gi|2065526|gb|U75698.1|KSU75698	98868	98979	112	98906	13			72
66	gi|2065526|gb|U75698.1|KSU75698	99295	99394	100	99327	13			73
67	gi|2065526|gb|U75698.1|KSU75698	104171	104284	114	104189	13			74

68	gi|2065526|gb|U75698.1|KSU75698	107171	107308	138	107224	14			52
69	gi|2065526|gb|U75698.1|KSU75698	110780	110890	111	110835	12			82
70	gi|2065526|gb|U75698.1|KSU75698	111692	111794	103	111756	17			25
71	gi|2065526|gb|U75698.1|KSU75698	112220	112319	100	112281	15			38
72	gi|2065526|gb|U75698.1|KSU75698	112666	112847	182	112821	14	ORF65		53
73	gi|2065526|gb|U75698.1|KSU75698	115937	116041	105	115983	18			18
74	gi|2065526|gb|U75698.1|KSU75698	116119	116277	159	116223	11			89
75	gi|2065526|gb|U75698.1|KSU75698	117034	117245	212	117068	11	ORF69	DE	90
76	gi|2065526|gb|U75698.1|KSU75698	117878	118441	564	117932	16			29
77	gi|2065526|gb|U75698.1|KSU75698	117878	118441	564	118171	29			6
78	gi|2065526|gb|U75698.1|KSU75698	117878	118441	564	118307	28			8
79	gi|2065526|gb|U75698.1|KSU75698	118895	119015	121	118944	14	K12	L	54
80	gi|2065526|gb|U75698.1|KSU75698	122562	122669	108	122613	13			75
81	gi|2065526|gb|U75698.1|KSU75698	123722	123866	145	123766	12			83
82	gi|2065526|gb|U75698.1|KSU75698	124500	125244	745	124659	23	ORF71-72	DE	12
83	gi|2065526|gb|U75698.1|KSU75698	124500	125244	745	124863	40			2
84	gi|2065526|gb|U75698.1|KSU75698	125294	125481	188	125368	18			19
85	gi|2065526|gb|U75698.1|KSU75698	125621	126468	848	125737	29			7
86	gi|2065526|gb|U75698.1|KSU75698	125621	126468	848	125951	28			9
87	gi|2065526|gb|U75698.1|KSU75698	125621	126468	848	126218	26			10
88	gi|2065526|gb|U75698.1|KSU75698	128393	128521	129	128450	15	ORF73	DE	39
89	gi|2065526|gb|U75698.1|KSU75698	129354	129453	100	129434	13			76
90	gi|2065526|gb|U75698.1|KSU75698	129756	129855	100	129805	14			55
91	gi|2065526|gb|U75698.1|KSU75698	130761	130860	100	130790	11			91

Table S1C. RBP-Jk (-VPA) peaks

Peak #	chr	start	end	length	abs_summit	pileup	Promoter	Kinetics	Rank by Height
1	gi|2065526|	484	583	100	577	8	ORF4	DE	40
2	gi|2065526|	859	1043	185	951	12	ORF4	DE	5
3	gi|2065526|	1191	1417	227	1352	10			11
4	gi|2065526|	2730	2853	124	2779	6	ORF6	DE	90
5	gi|2065526|	3418	3517	100	3469	7			68
6	gi|2065526|	5185	5477	293	5377	9			23
7	gi|2065526|	6805	6904	100	6885	8			41
8	gi|2065526|	7487	7635	149	7544	10			12
9	gi|2065526|	8276	8406	131	8316	9	ORF8	DE	24
10	gi|2065526|	9329	9428	100	9362	8			42
11	gi|2065526|	9475	9756	282	9585	13			2
12	gi|2065526|	14000	14160	161	14084	8			43
13	gi|2065526|	16325	16449	125	16389	10			13
14	gi|2065526|	16595	16694	100	16670	8			44
15	gi|2065526|	17276	17486	211	17377	10			14
16	gi|2065526|	18421	18520	100	18499	6	vIL6	DE	91
17	gi|2065526|	19553	19728	176	19618	9	K3-int		25
18	gi|2065526|	20302	20406	105	20355	10	ORF70-K3	DE	15
19	gi|2065526|	21287	21488	202	21336	8			45
20	gi|2065526|	25112	25220	109	25172	7			69
21	gi|2065526|	27774	27873	100	27829	7	K6/K6.2/K7/PAN	DE/DE/DE/DE	70
22	gi|2065526|	28282	28381	100	28365	6	K6/K6.2/PAN	DE/DE	92
23	gi|2065526|	29003	29256	254	29199	10	ORF16	DE	16
24	gi|2065526|	29453	29619	167	29508	8	ORF16	DE	46
25	gi|2065526|	35840	35982	143	35904	7			71
26	gi|2065526|	36346	36564	219	36415	10			17
27	gi|2065526|	36762	36933	172	36828	12			6
28	gi|2065526|	37493	37592	100	37563	7			72
29	gi|2065526|	38852	38977	126	38907	9			26
30	gi|2065526|	43575	43708	134	43688	8			47
31	gi|2065526|	44229	44345	117	44279	11			9
32	gi|2065526|	44610	44741	132	44661	6			93
33	gi|2065526|	46744	46892	149	46819	9	ORF26/27	L/L	27
34	gi|2065526|	47932	48183	252	48013	8	ORF28	L	48
35	gi|2065526|	49545	49673	129	49593	7			73
36	gi|2065526|	50435	50691	257	50620	9			28
37	gi|2065526|	53127	53226	100	53183	8			49
38	gi|2065526|	56940	57128	189	57068	8			50
39	gi|2065526|	57727	57847	121	57778	10	ORF38	DE	18
40	gi|2065526|	58784	59007	224	58932	9			29
41	gi|2065526|	59671	59772	102	59720	6			94
42	gi|2065526|	60048	60242	195	60134	7			74
43	gi|2065526|	60759	60858	100	60838	7	ORF39	DE	75
44	gi|2065526|	62267	62369	103	62316	9			30
45	gi|2065526|	63938	64148	211	64076	8			51
46	gi|2065526|	64383	64558	176	64532	8			52
47	gi|2065526|	65705	65914	210	65753	8			53
48	gi|2065526|	66284	66383	100	66328	10			19
49	gi|2065526|	66892	67021	130	66971	8			54
50	gi|2065526|	67060	67186	127	67120	6			95
51	gi|2065526|	69436	69628	193	69497	9	ORF45/45.1/50	DE/DE/DE	31
52	gi|2065526|	69996	70360	365	70145	12	ORF46-57/50	DE/DE	7
53	gi|2065526|	70795	70981	187	70880	9	ORF46-57/50	DE/DE	32
54	gi|2065526|	71288	71533	246	71443	9	ORF50	DE	33
55	gi|2065526|	72294	72503	210	72446	7			76

56	gi|2065526|	72787	72886	100	72834	9			34
57	gi|2065526|	73996	74141	146	74072	8	KbZIP	DE	55
58	gi|2065526|	74376	74552	177	74470	8	KbZIP	DE	56
59	gi|2065526|	74641	74925	285	74757	18	ORF50AS/KbZIP	DE/DE	1
60	gi|2065526|	75044	75185	142	75124	7	ORF50AS/K8.1	DE/DE	77
61	gi|2065526|	76532	76713	182	76628	7			78
62	gi|2065526|	79032	79145	114	79080	7	ORF55	DE	79
63	gi|2065526|	81087	81221	135	81171	7	ORF57	DE	80
64	gi|2065526|	83159	83280	122	83228	8			57
65	gi|2065526|	83604	83738	135	83669	8			58
66	gi|2065526|	85539	85679	141	85625	7			81
67	gi|2065526|	88647	88809	163	88747	8			59
68	gi|2065526|	89599	89729	131	89648	6			96
69	gi|2065526|	89872	90070	199	89941	7			82
70	gi|2065526|	92583	92712	130	92643	10			20
71	gi|2065526|	93076	93184	109	93125	8			60
72	gi|2065526|	93514	93613	100	93542	8			61
73	gi|2065526|	95118	95279	162	95204	12			8
74	gi|2065526|	98078	98197	120	98143	9			35
75	gi|2065526|	98258	98526	269	98330	10			21
76	gi|2065526|	98568	98775	208	98620	8			62
77	gi|2065526|	99643	99760	118	99693	7			83
78	gi|2065526|	102872	102999	128	102932	7			84
79	gi|2065526|	103101	103315	215	103235	11			10
80	gi|2065526|	105405	105504	100	105476	8			63
81	gi|2065526|	111210	111353	144	111286	7			85
82	gi|2065526|	111576	111734	159	111653	9			36
83	gi|2065526|	112334	112453	120	112385	10			22
84	gi|2065526|	116012	116111	100	116076	7			86
85	gi|2065526|	117218	117415	198	117307	7			87
86	gi|2065526|	118253	118355	103	118301	8			64
87	gi|2065526|	124750	125022	273	124888	13			3
88	gi|2065526|	126099	126198	100	126145	6			97
89	gi|2065526|	126724	126923	200	126806	8			65
90	gi|2065526|	128359	128483	125	128392	8	ORF73	DE	66
91	gi|2065526|	128759	128874	116	128824	9	ORF73	DE	37
92	gi|2065526|	129364	129463	100	129407	7			88
93	gi|2065526|	129701	129811	111	129777	8			67
94	gi|2065526|	130096	130195	100	130143	9			38
95	gi|2065526|	131369	131468	100	131444	7			89
96	gi|2065526|	132435	132666	232	132576	9			39
97	gi|2065526|	137377	137508	132	137469	13			4

Table S1D. Rta (+VPA) and RBP-Jk peaks: co-localized or in same promoters

Rta Peak #	abs_summit	Promoter	Kinetics	RBP-Jk (+VPA) Peak #	abs_summit	Promoter	Kinetics	RBP-Jk (-VPA) Peak #	abs_summit	Promoter	Kinetics
5	2716	ORF6	DE	3	2704	ORF6	DE				
9	6158			6	6139						
21	28355	K6/K6.2/PAN	DE/DE/DE					22	28365	K6/K6.2/PAN	DE/DE/DE
25	30125			18	30107						
30	39611			23	39634						
51	70086	ORF45.1/46-47/50	DE/DE/DE	39	70059	ORF45.1/46-47/50	DE/DE/DE				
52	70284	ORF46-47/50	DE/DE	40	70283	ORF46-47/50	DE/DE				
53	71004	ORF50	DE	42	71015	ORF50	DE				
54	71410	ORF50	DE	44	71435	ORF50	DE	54	71443	ORF50	DE
57	74720	ORF50AS/KbZIP	DE/DE	53	74719	ORF50AS/KbZIP	DE/DE	59	74757	ORF50AS/KbZIP	DE/DE
58	75151	ORF50AS/K8.1	DE/L					60	75124	ORF50AS/K8.1	DE/L
64	81901	ORF57	DE	57	81962	ORF57	DE				
69	92700							70	92643		
90	118176			77	118171						
98	124873			83	124863			87	124888		
100	125758			85	125737						

Green font=RBP-Jk increased in reactivation
Red font=RBP-Jk decreased in reactivation

Same promoter but not co-localized

15	18302	vIL6	DE	12	18756	vIL6	DE				
22	28617	K6/PAN	DE/DE	17	27853	K6/K6.2/K7/PAN	DE/DE/DE/DE				
49	69005	ORF45/50	DE/DE								
50	69618	ORF45/45.1/50	DE/DE/DE	38	69850	ORF45/45.1/50	DE/DE/DE				
92	119190	K12	L	79	118944	K12	L				
102	128326	ORF73	DE	88	128450	ORF73	DE	90	128392	ORF73	DE
								91	128824	ORF73	DE

Table S2. Classification of RBP-Jk peaks in latency and reactivation of KSHV: data. Green text=RBP-Jk peak increased in reactivation, red text=RBP-Jk peak decreased in reactivation. Abbreviations: abs_summit=peak summit, pileup=height in read depth of peak summit, fold change in pileup=reactivation (+VPA) pileup/latency (-VPA) pileup, used to determine classifications for latency/reactivation peaks. RBP-Jk class # corresponds to Table 2.

Table S2. Classification of RBP-Jk peaks

RBP-Jk (VPA-) Peak #	abs_summit	pileup	Promoter	Kinetics	RBP-Jk (VPA+) Peak #	abs_summit	pileup	Promoter	Kinetics	# -VPA SDs	RBP-Jk Class #
1	577	8	ORF4	DE							5
2	951	12	ORF4	DE							5
3	1352	10									5
					1	1687	12				2
					2	2295	13	ORF6	DE		2
					3	2704	12	ORF6	DE		2
4	2779	6	ORF6	DE							5
5	3469	7									5
					4	4508	14				2
					5	4837	14				2
6	5377	9									5
					6	6139	16				2
					7	6346	13				2
7	6885	8									5
8	7544	10									5
9	8316	9	ORF8	DE	8	8294	15	ORF8	DE	-0.41	1
					9	8471	17	ORF8	DE		2
10	9362	8									5
11	9585	13									5
					10	11553	14				2
12	14084	8									5
					11	15540	17	ORF11	DE		2
13	16389	10									5
14	16670	8									5
15	17377	10									5
16	18499	6	vIL6	DE							5
					12	18756	14	vIL6	DE		2
					13	19267	14	K3-int	DE		2
17	19618	9	K3-int	DE							5
18	20355	10	ORF70-K3	DE							5
19	21336	8									5
					14	24350	22				2
					15	24521	23				2
20	25172	7									5
					16	25400	14				2
21	27829	7	K6/K6.2/K7/PAN	DE/DE/DE/DE	17	27853	13	K6/K6.2/K7/PAN	DE/DE/DE/DE	-0.08	1
22	28365	6	K6/K6.2/PAN	DE/DE							5
23	29199	10	ORF16	DE							5
24	29508	8	ORF16	DE							5
					18	30107	15				2
					19	31443	13				2
25	35904	7									5
26	36415	10			20	36446	11			-1.60	4
27	36828	12									5
28	37563	7									5
					21	38156	11				2
					22	39406	13				2
29	38907	9									5
					23	39634	15				2
					24	39906	16				2
					25	40816	13				2
30	43688	8									5
					26	43867	17				2
31	44279	11									5
32	44661	6									5
33	46819	9	ORF26/27	L/L							5
34	48013	8	ORF28	L							5
					27	48127	13	ORF28	L		2
35	49593	7									5
36	50620	9			28	50655	14			-0.62	1
					29	52812	11				2
37	53183	8									5
					30	53756	13	ORF34	DE		2
					31	53999	15	ORF34	DE		2
					32	56375	15				2
38	57068	8									5
					33	57561	11	ORF38	DE		2
39	57778	10	ORF38	DE							5
40	58932	9									5
					34	59305	12				2
41	59720	6									5
42	60134	7									5

43	60838	7	ORF39	DE						5
44	62316	9								5
45	64076	8								5
46	64532	8								5
					35	65531	15			2
47	65753	8								5
					36	66173	15			2
48	66328	10								5
49	66971	8								5
50	67120	6								5
					37	67340	14			2
51	69497	9	ORF45/45.1/50	DE/DE/DE						5
					38	69850	14	ORF45/45.1/50	DE/DE/DE	2
					39	70059	18	ORF45.1/46-47/50	DE/DE/DE	2
52	70145	12	ORF46-47/50	DE/DE						5
					40	70283	20	ORF46-47/50	DE/DE	2
					41	70615	13	ORF46-47/50	DE/DE	2
53	70880	9	ORF46-47/50	DE/DE						5
					42	71015	14	ORF50	DE	2
					43	71287	14	ORF50	DE	2
54	71443	9	ORF50	DE	44	71435	21	ORF50	DE	-0.81 1
					45	71575	17			2
					46	71779	13			2
55	72446	7								5
					47	72642	15			2
56	72834	9								5
					48	73128	17			2
					49	73423	12			2
57	74072	8	KbZIP	DE	50	74098	35	KbZIP	DE	4.04 3
					51	74283	32	KbZIP	DE	2
58	74470	8	KbZIP	DE	52	74452	38	KbZIP	DE	4.65 3
59	74757	18	ORF50AS/KbZIP	DE/DE	53	74719	42	ORF50AS/KbZIP	DE	1.79 3
60	75124	7	ORF50AS/K8.1	DE/DE						5
					54	75204	14	ORF50AS/K8.1	DE/L	2
61	76628	7								5
					55	78858	13	ORF55	DE	2
62	79080	7	ORF55	DE						5
63	81171	7	ORF57	DE						5
					56	81596	16	ORF57	DE	2
					57	81962	13	ORF57	DE	2
64	83228	8								5
65	83669	8			58	83612	21			1.18 3
66	85625	7								5
					59	86184	11			2
					60	88484	12			2
67	88747	8								5
68	89648	6								5
69	89941	7								5
					61	90936	13			2
70	92643	10								5
					62	92760	13			2
					63	92948	13			2
71	93125	8			64	93068	13			-0.45 1
72	93542	8								5
73	95204	12								5
74	98143	9								5
75	98330	10								5
76	98620	8								5
					65	98906	13			2
					66	99327	13			2
77	99693	7								5
78	102932	7								5
79	103235	11								5
					67	104189	13			2
80	105476	8								5
					68	107224	14			2
					69	110835	12			2
81	111286	7								5
82	111653	9								5
					70	111756	17			2
					71	112281	15			2
83	112385	10								5
					72	112821	14	ORF65	L	2
					73	115983	18			2
84	116076	7								5
					74	116223	11			2

						75	117068	11	ORF69	DE	2
85	117307	7									5
						76	117932	16			2
						77	118171	29			2
86	118301	8				78	118307	28		2.60	3
						79	118944	14	K12	L	2
						80	122613	13			2
						81	123766	12			2
						82	124659	23	ORF71-72	DE	2
87	124888	13				83	124863	40		3.22	3
						84	125368	18			2
						85	125737	29			2
						86	125951	28			2
88	126145	6									5
						87	126218	26			2
89	126806	8									5
90	128392	8	ORF73	DE		88	128450	15	ORF73	DE	-0.04	1
91	128824	9	ORF73	DE								5
92	129407	7				89	129434	13			-0.08	1
93	129777	8				90	129805	14			-0.25	1
94	130143	9										5
						91	130790	11				2
95	131444	7										5
96	132576	9										5
97	137469	13										5

Table S3. Orphan Motifs over-represented at RBP-Jk peaks at early promoters

	Orphan motif[d]					
	1	2	3	4	5	6
Jk 2/ Jk 5 [a]	6.7 (0.018)	5.8 (0.03)	5.7 (4e-7)	2.6 (0.006)	-3.2 (0.006)	-2.6 (0.03)
Jk 2+Rta/ Jk 2 [b]	2.2 (0.018)	1.5 (0.47)	0 (4e-6)	2.9 (0.08)	1.2 (0.41)	0 (0.06)
# of promoters[c]	7	6	12	6	15	10

[a] number of motifs <61 bp to RBP-Jk Class 2 peak ("Jk2") divided by number of motifs <61 bp to RBP-Jk Class 5 ("Jk5") peak in early promoters, expressed as fold relative to actual ratio of Jk2/Jk5 peaks, which was 1.2. Number in parentheses is Z-test p value compared to observed ratio of peaks.

[b] number of motifs <61 bp to RBP-Jk Class 2 peak/Rta peak ("Jk2+Rta") divided by number of motifs <61 bp to RBP-Jk Class 2 ("Jk2") peak in early promoters, expressed as fold relative to actual ratio of Jk2+Rta/Rta peaks, which was 0.28. Number in parentheses is Z-test p value compared to observed ratio of peaks; "NA"=not applicable

[c] number of promoters with co-localized Class 2 or Class 5 RBP-Jk peak

[d] Orphan motifs numbered consecutively.

Table S4. Localization of dual Rta-c/POU Motifs at RBP-Jk and Rta peaks at early promoters

	Rta-c Motif + POU Motif [d]				
	POU2F3	P5F1B	POU3F4	Oct-v	POU4F2
Jk 2/ Jk 5 [a]	inf	inf	inf	12.3	1.1
Jk 2+Rta/ Jk 2 [b]	3.8	null	1.6	3.0	2.3
# of promoters [c]	4	1	2	7	5

[a] number of Rta-c/POU motifs <61 bp to RBP-Jk Class 2 ("Jk2") peaks divided by number of motifs <61 bp to RBP-Jk Class 5 peaks ("Jk5") in early promoters, expressed as fold relative to actual ratio of Jk2/Jk5 peaks, which was 1.2. "inf"=0 Jk5 peaks

[b] number of motifs <61 bp to RBP-Jk Class 2 peak/Rta peaks ("Jk2+Rta") divided by number of motifs <61 bp to RBP-Jk Class 2 peaks ("Jk2") in early promoters, expressed as fold relative to actual ratio of Jk2+Rta/Jk2 peaks, which was 0.28.

[c] number of promoters with co-localized Class 2 or Class 5 RBP-Jk peak

[d] Rta-c motifs coincident with the indicated POU Motifs (consensus from Homo Sapiens Comprehensive Model Collection (HOCOMOCO) (68,69)).