Table S1. SAXS data collection and analysis parameters. Program version numbers are shown in parentheses.

	pUL7:pUL51		pUL7:pUL51 (8-142)
	1:2 complex	2:4 complex	1:2 complex
Data-collection parameters			
Radiation Source	Petra III (DESY, Hamburg, Germany)		
Beamline	EMBL P12		
Detector	Dectris Pilatus 6M		
Beam geometry (mm)	0.2 × 0.12		
X-ray wavelength (nm)	0.124		
Sample-to-detector distance (m)	3.0		
Temperature (°C)	20.2		
Measured *s*-range (nm^{-1})	0.0225–7.299		
Exposure time (s)	0.995		
Injected protein concentration (mg/mL)	8		4.5
Shannon-channel limited *s*-range (nm^{-1})	< 5.57	< 6.70	< 7.16
Structural parameters			
I(0) (a.u.*) [from *p*(*r*)]	4624 ± 13	3136 ± 11	3098 ± 5
Real-space *R* g (nm) [from *p*(*r*)]	4.30 ± 0.03	4.79 ± 0.04	3.0 ± 0.01
I(0) (a.u.*) (from Guinier)	4538 ± 10	3100 ± 7	3331 ± 2
R_g (nm) (from Guinier)	3.95 ± 0.07	4.56 ± 0.28	2.96 ± 0.01
D_{max} (nm)	18.2	19.7	11.5
Porod volume estimate (Vp, nm^3)	160	340	116
Molecular-mass determination			
Molecular mass M_r, kDa [from SAXSMOW]	95	177	73
Molecular mass M_r, kDa [from Vc]	81	167	66
Molecular mass M_r, kDa [from Bayesian consensus]	86–96	162–195	66–73
Expected M_r from sequence, kDa	84.37	168.7	63.11
Software employed			
Primary data reduction	*CHROMIXS*		
Data processing	*PrimusQT/GNOM(5.0)*		
Ab initio analysis	*DAMMIN(5.3)/GASBOR(2.3i)*		
Spatial averaging and resolution estimates	*DAMAVER(5.0)*		
Computation of model intensities	*CRYSOL(2.8.3)*		
Pseudo-atomic modelling	*CORAL(1.1)*		
Small Angle Scattering Biological Data Bank			
SASBDB accession codes	SASDG57	SASDG47	SASDG37

*arbitrary units

Table S2. Crystallographic data collection and refinement statistics. Statistics for the highest-resolution shell are shown in parentheses.

		Mercury(II) acetate derivative			
	Native	Remote (High E)	Peak	Inflection	Remote (Low E)
Data collection					
Wavelength (Å)	0.97625	0.99702	1.00728	1.00809	1.01627
Space group	$P\,2_1$		$P\,4\,2_1\,2$		
Cell dimensions					
a, b, c (Å)	79.51, 106.3, 106.0	106.5, 106.5, 79.0	106.5, 106.5, 79.2	106.5, 106.5, 79.3	106.5, 106.5, 79.4
α, β, γ (°)	90, 92.0, 90	90, 90, 90	90, 90, 90	90, 90, 90	90, 90, 90
Resolution (Å)	105.9–1.8 (1.86–1.83)	53.2–2.8 (2.96–2.80)	53.2–2.9 (3.02–2.87)	53.3–2.9 (3.09–2.91)	53.3–3.0 (3.16–2.98)
Unique reflections	154,984 (7654)	11,618 (1627)	10,931 (1561)	10,498 (1643)	9789 (1515)
Completeness (%)	100 (99.9)	99.7 (97.9)	99.9 (99.5)	99.9 (99.7)	99.7 (98.5)
Anomalous	–	99.7 (97.9)	99.9 (99.5)	99.9 (99.7)	99.7 (98.5)
Multiplicity	6.5 (6.5)	47.6 (36)	24.9 (25.6)	24.8 (24.9)	24.7 (24.8)
Anomalous	–	25.9 (19.1)	13.5 (13.5)	13.5 (13.2)	13.5 (13.2)
R_{merge}	0.120 (3.197)	0.261 (2.664)	0.231 (2.506)	0.235 (2.348)	0.232 (2.158)
R_{pim}	0.051 (1.367)	0.038 (0.435)	0.047 (0.502)	0.048 (0.476)	0.047 (0.439)
$CC_{1/2}$	0.996 (0.321)	0.999 (0.804)	0.999 (0.783)	0.999 (0.792)	0.999 (0.809)
CC_{anom}	–	0.830 (0.059)	0.741 (0.000)	0.664 (0.014)	0.224 (0.000)
Mean I/σ(I)	6.8 (0.5)	14.3 (1.7)	12.1 (1.6)	12.4 (1.7)	12.4 (1.8)
Wilson B (A^2)	35.2				
Refinement					
Resolution (Å)	26.6–1.8 (1.84–1.83)				
Reflections					
Working set	154,885 (2892)				
Test set	8093 (206)				
R_{work}	0.194 (0.240)				
R_{free}	0.220 (0.244)				
No. of atoms					
Protein	11692				
Solvent	717				
Other*	28				
Root mean square deviation					
Bond lengths (Å)	0.009				
Bond angles (°)	0.90				
Ramachandran favoured (%)	98.7				
Ramachandran outliers (%)	0.0				
Poor rotamers (%)	0.39				
Mean B value (A^2)	45.2				

*Glycerol molecules and chloride ions

Table S3. pUL7:pUL51(8–142) cross-links identified by mass spectrometry. Two protein bands from SDS-PAGE analysis, with molecular masses corresponding to 1:1 and 1:2 pUL7:pUL51(8–142), were analyzed.

Reagent	Band	Protein	Residue	Sequence	Protein	Residue	Sequence
DSBU	1:1	pUL7	17	AAATADDEGSA-ATIL[**K**]QAIAGDR	pUL51	107	HHPGLEAPTIDG-AVAAHQD[**K**]MR
DSBU	1:1	pUL51	67	RLV[**K**]AR	pUL51	67	LV[**K**]AR
DSBU	1:1	pUL7	285	APLVYWWLSETP[**K**]R	pUL51	67	LV[**K**]AR
DSBU	1:2	pUL51	67	RLV[**K**]AR	pUL51	67	LV[**K**]AR
DSSO	1:1	pUL7	91	FVLDGSPEDAYVTSEDYF[**K**]R	pUL51	67	LV[**K**]AR
DSSO	1:1	pUL7	17	AAATADDEGSA-ATIL[**K**]QAIAGDR	pUL51	107	HHPGLEAPTIDG-AVAAHQD[**K**]MRR
DSSO	1:1	pUL51	107	HHPGLEAPTIDGAVAAHQD[**K**]MR	pUL51	67	RLV[**K**]AR
DSSO	1:1	pUL7	163	SHATPSTFA[**K**]VLAWLGVAGR	pUL51	67	LV[**K**]AR
DSSO	1:1	pUL51	131	LADTCMATILQMYMSV-GAAD[**K**]SADVLVSQAIR	pUL51	67	RLV[**K**]AR
DSSO	1:1	pUL7	17	AAATADDEGSA-ATIL[**K**]QAIAGDR	pUL51	67	LV[**K**]AR

Table S4. Co-evolution of the pUL7-pUL51 interaction interface across *Alphaherpesvirinae*. *z* is the sum of correlation values for interacting residue pairs and *p* is the probability that this value would be expected by chance. The selection of sequences for each data set is described in *Materials and Methods*.

			No. of interacting residues			
Data set	No. strains, *N*	No. interactions, *I*	pUL51	pUL7	*z*	*p*
1	199	35	21	19	4301.24	0.061
2	197	54	27	29	7319.44	0.068
3	197	52	26	28	6969.40	0.065
4	197	38	22	21	4559.47	0.062