	ICP0 LE	ICP0 HE	His-ICP0
Data Collection			
Unit-cell parameters (Å, °)	*a*=*b*=96.60, *c*=75.33	*a*=*b*=95.91, *c*=74.53	*a*=*b*=95.15, *c*=76.72
Space group	$P4_12_12$	$P4_12_12$	$P4_12_12$
Resolution (Å)†	46.36-3.00 (3.18-3.00)	47.95-2.65 (2.78-2.65)	43.45-2.45 (2.55-2.45)
Wavelength (Å)	1.5895	1.0000	1.0000
Temperature (K)	100	100	100
Observed reflections	171,401	134,156	89,786
Unique reflections	7,423	10,603	14,026
$\langle I/(\sigma I)\rangle$†	13.1 (1.7)	14.6 (1.9)	13.1 (1.6)
Completeness (%)†	98.0 (100)	100 (99.9)	99.9 (100)
Multiplicity†	23.1 (24.9)	12.7 (13.4)	6.4 (6.3)
R_{merge} (%)†, ‡	27.6 (263.8)	12.3 (145.2)	11.3 (92.6)
R_{meas} (%)†, ¶	28.2 (269.3)	12.8 (150.7)	12.4 (101.2)
R_{pim} (%)†, ¶	5.8 (53.6)	3.6 (41.0)	4.8 (40.2)
$CC_{1/2}$ †, ‖	0.997 (0.749)	0.999 (0.862)	0.998 (0.714)
DelAnom CC#	0.333	0.067	
Refinement			
Resolution (Å)†		34.73-2.65	43.45-2.45
Reflections (working/test)†		10,033/511	13,323/667
R_{factor} / R_{free} (%)†,§		21.8/28.8	19.2/25.4
No. of atoms (Protein/Iodide/water)		1,684/2/-	1,743/3/42
Model Quality			
R.m.s deviations			
Bond lengths (Å)		0.009	0.009
Bond angles (°)		1.136	0.991
Average *B*-factor (Å^2)			
All Atoms		71.2	44.8
Protein		71.2	44.8
Iodide		106.42	58.5
Water		-	42.2
Coordinate error (maximum likelihood) (Å)		0.35	0.34

Ramachandran Plot		
Most favored (%)	97.7	97.8
Additionally allowed (%)	2.3	2.2

Supplemental Table 1: Crystallographic data for ICP0.

† Values in parenthesis are for the highest resolution shell.

‡ $R_{merge} = {}_{hkli} \, |I_i(hkl) - \langle I(hkl) \rangle| \, / \, {}_{hkli} \, I_i(hkl)$, where $I_i(hkl)$ is the intensity measured for the ith reflection and $\langle I(hkl) \rangle$ is the average intensity of all reflections with indices hkl.

§ $R_{factor} = {}_{hkl} \, ||F_{obs}(hkl)| - |F_{calc}(hkl)|| \, / \, {}_{hkl} \, |F_{obs}(hkl)|$; Rfree is calculated in an identical manner using 5% of randomly selected reflections that were not included in the refinement.

¶ R_{meas} = redundancy-independent (multiplicity-weighted) R_{merge}[1,2]. R_{pim} = precision-indicating (multiplicity-weighted) R_{merge}[3,4].

|| $CC_{1/2}$ is the correlation coefficient of the mean intensities between two random half-sets of data[5,6].

DelAnom CC is the correlation coefficient between the Bijvoet differences ($I_{(hkl)} - I_{(-h-k-l)}$) from two random half-sets of data[1] and is used to estimate the anomalous signal strength.

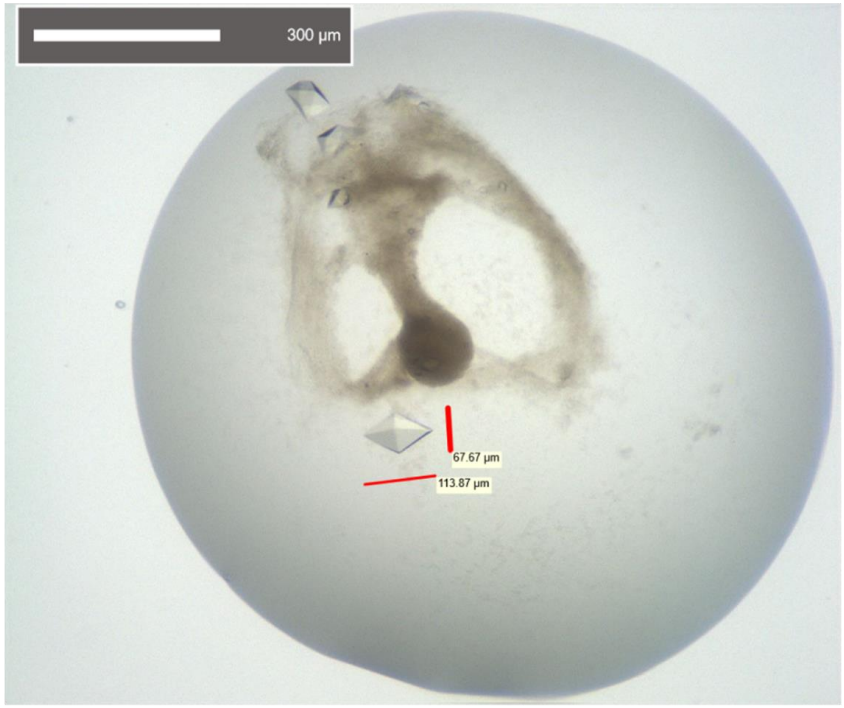
β-strand group	Residue N-Atom	Residue O-Atom	Distance (Å)
βG1	Y643	L747	2.96
	L644	V653	2.91
	I646	S651	3.01
	L653	L644	2.85
	M734	G738	2.83
	G738	M734	2.69
	M740	L732	2.84
	L741	V748	2.76
	D743	T746	2.79
	T746	D743	2.82
	V748	L741	2.95
βG2	D666	L684	2.98
	L668	V682	2.77
	I670	A680	2.92
	D672	N677	3.06
	G676	D672	2.84
	V682	L668	2.84
	L684	D666	2.88
βG3	H715	R759	2.99
	T717	R757	2.74
	R759	H715	2.87

Supplemental Table 2: Backbone hydrogen bond interactions in the β-strand regions of the ICP0 C-terminal dimer domain.

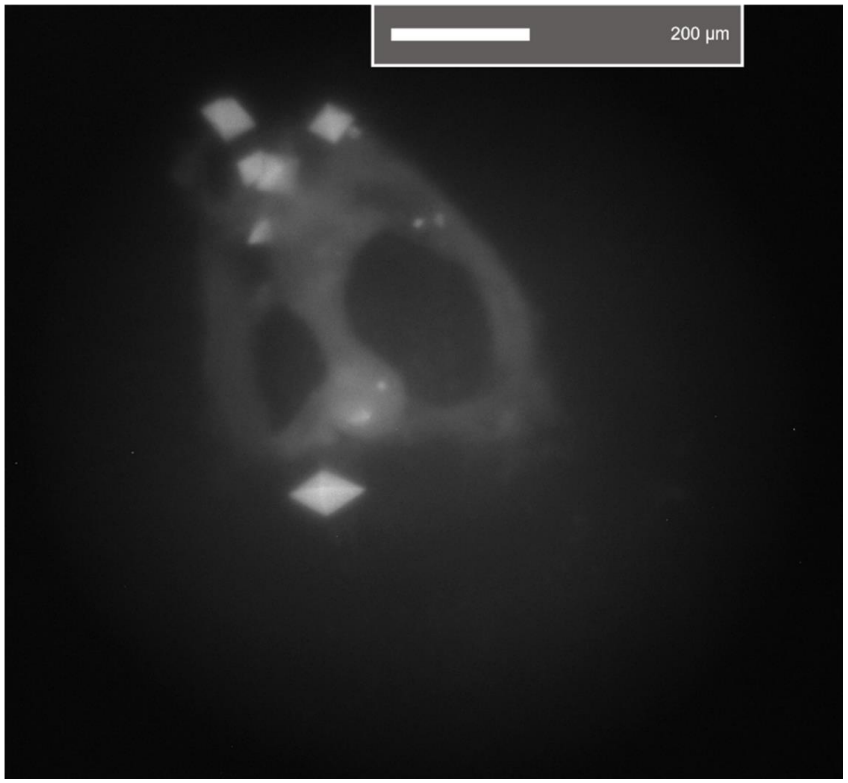
Subunit: AB Residue/Atom	Subunit: CD Residue/Atom	Distance (Å)
A: S731/N	D: N739/OD1	2.8
A: W733/N	D: M740/O	2.84
A: G745/N	D: S650/OG	2.68
B: T735/N	C: N730/OD1	2.98
B: M740/N	C: S731/O	3.08
B: F742/N	C: W733/O	3.01
B: Q744/N	D: E674/OE2	2.87
B: N739/OD1	C: S739/N	2.8
B: M740/O	C: W733/N	2.84
B: S650/OG	C: G745/N	2.68
A: N730/OD1	D: T735/N	2.98
A: S731/O	D: M740/N	3.08
A: W733/O	D: F742/N	3.01
B: E764/OE2	D: Q744/N	2.87

Supplemental Table 3: Hydrogen bond interactions between subunits in the ICP0 tetramer (dimer of dimers). Highlighted interactions occur between the β6-β7 strands.

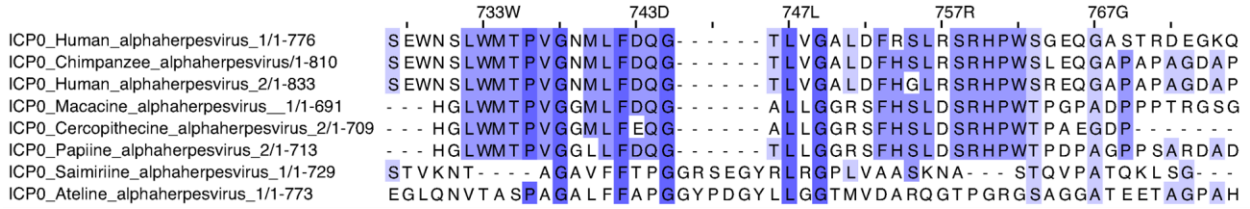
A



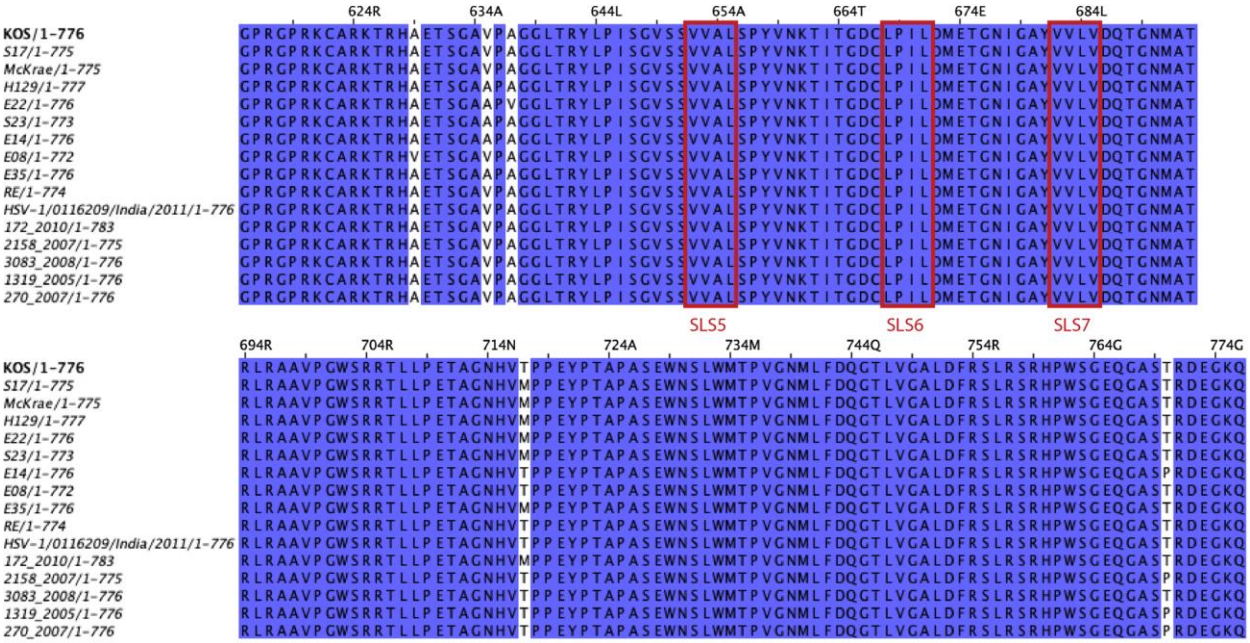
B



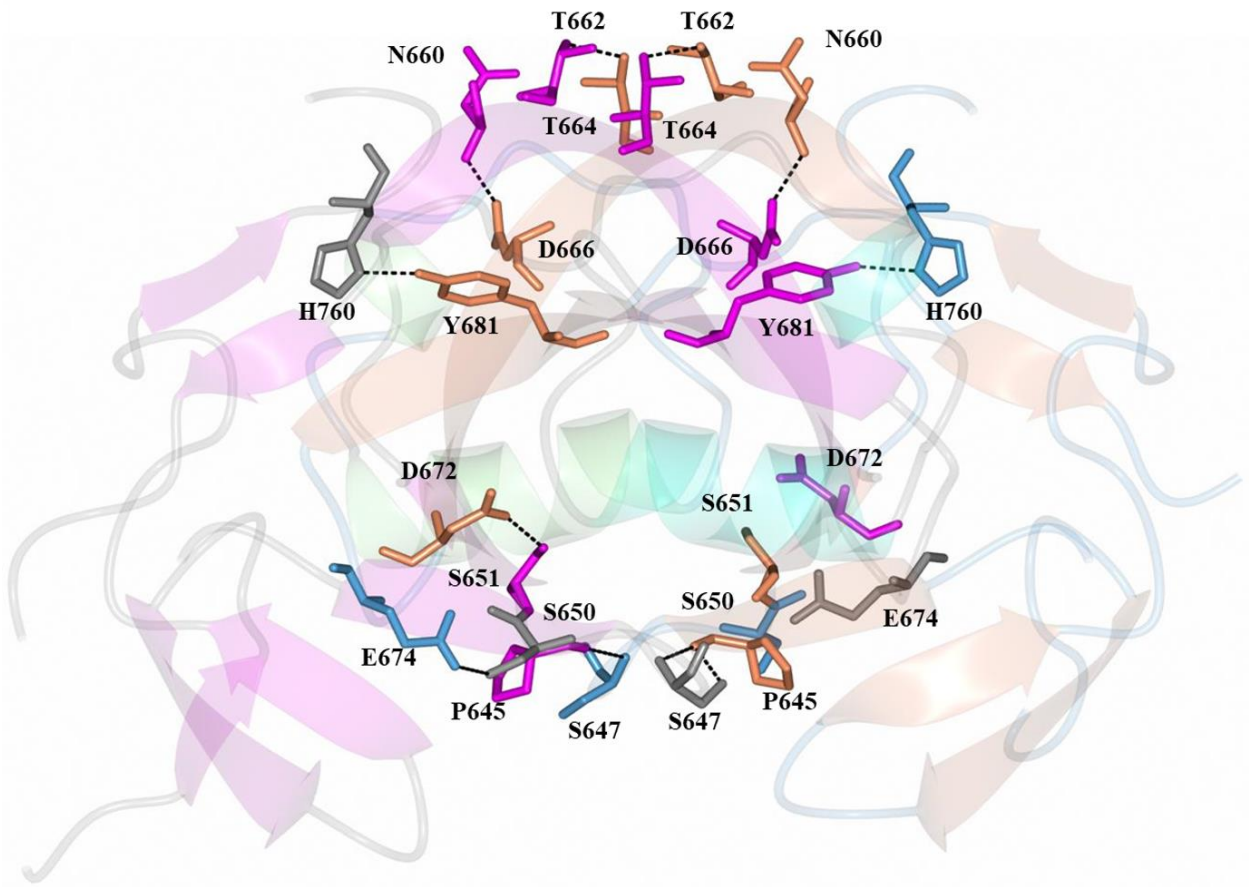
Supplemental Figure 1: Crystals of ICP0. **A)** Visible light image and **B)** UV fluorescence image.



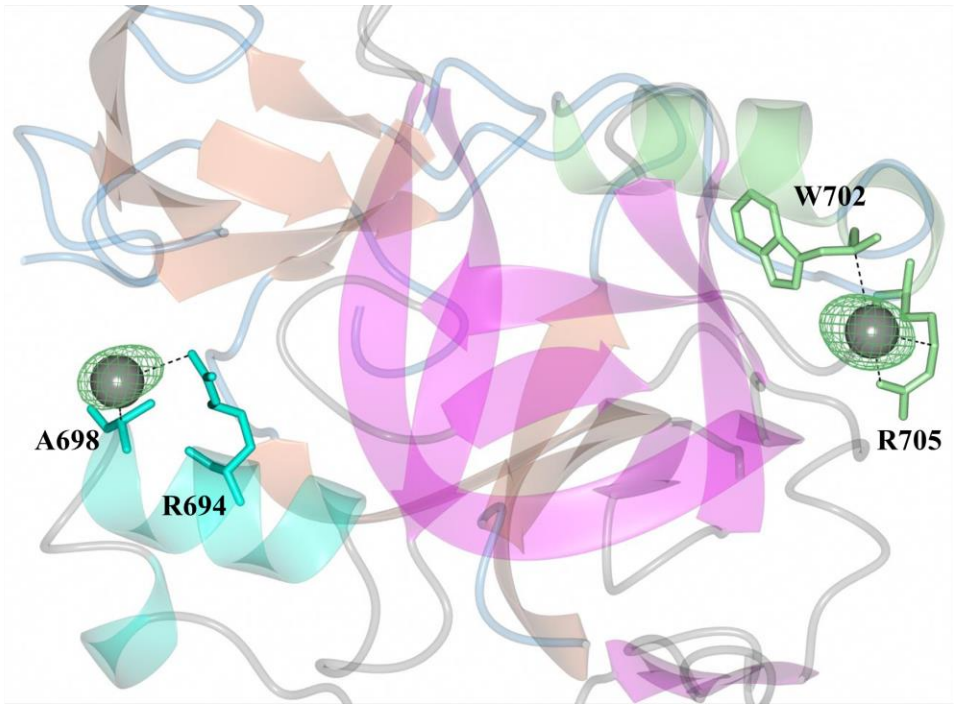
Supplemental Figure 2: Alignment of ICP0 CTD tetramer interface residues of unique herpesvirus species containing the CTD. The numbering is relative to the HSV-1 ICP0.



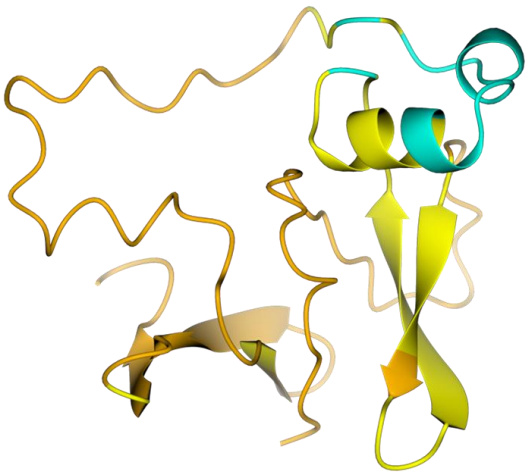
Supplemental Figure 3: Alignment of full ICP0 CTD of HSV-1 strains and clinical isolates. The full ICP0 CTD of various HSV-1 strains and clinical isolates. The numbering is relative to the HSV-1 ICP0 KOS strain.



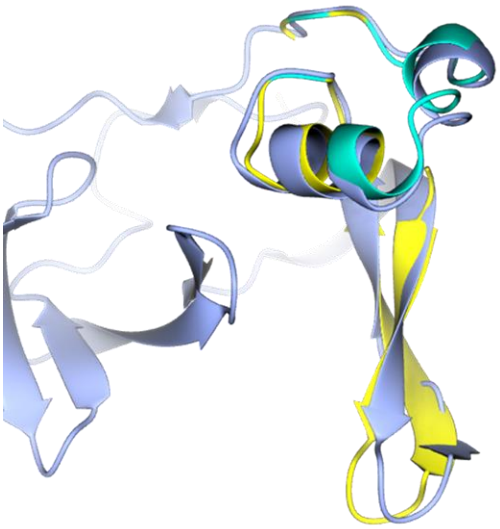
Supplemental Figure 4: Side chain hydrogen bond interaction between subunits (dashed lines). Subunit A helices (cyan), β-strands (magenta) and loops (gray). Subunit B helices (green), β-strands (tan) and loops (blue).



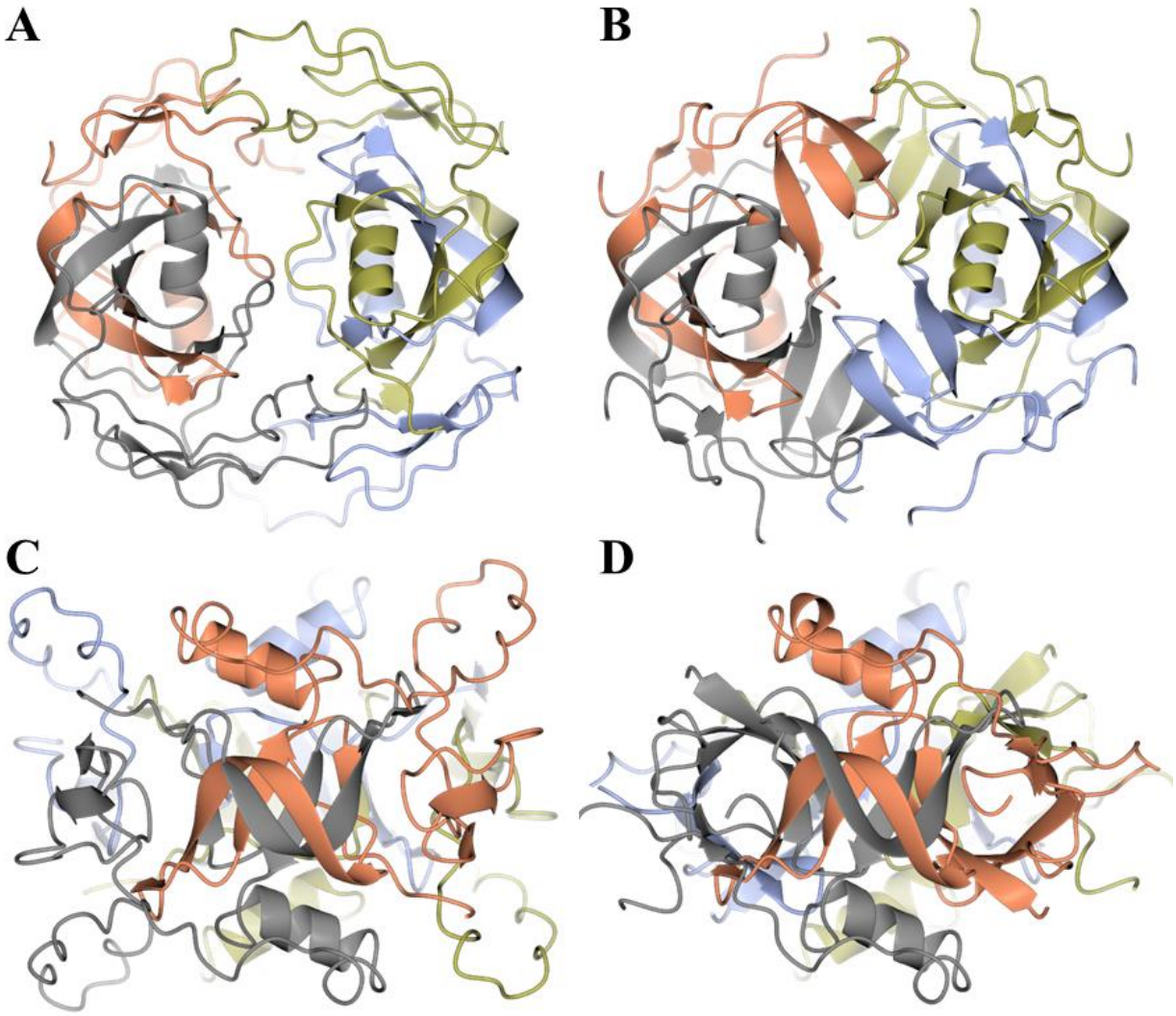
Supplemental Figure 5: Phased anomalous difference map (green mesh) contoured at 3 showing the positions of the iodide ions (gray spheres). The dashed lines indicated close contacts between 3.6-3.9 Å.



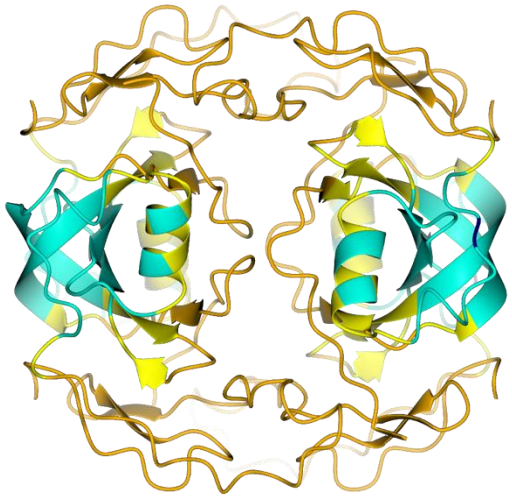
Supplemental Figure 6: Alphafold model of the monomeric ICP0 CTD. The Alphafold model of the ICP0 CTD is shown in ribbons, colored by the pLDDT (confidence): confident (cyan, 90 > pLDDT > 70), low (yellow, 70 > pLDDT > 50), and very low (orange, pLDDT < 50).



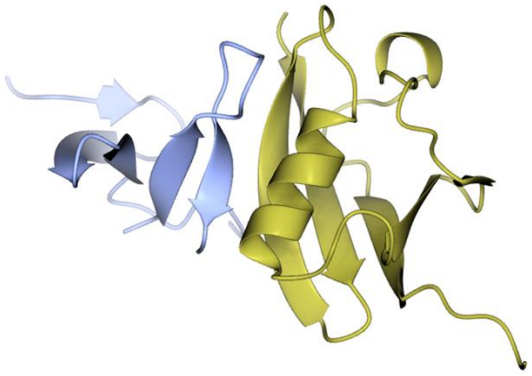
Supplemental Figure 7: The region of the Alphafold model of the monomeric ICP0 CTD with low or moderate confidence recapitulates the monomeric structure. The Alphafold model of the ICP0 CTD with pLDDT > 50 is shown in ribbons (cyan, 90 > pLDDT > 70 vs yellow, 70 > pLDDT > 50). A single chain of the ICP0 CTD is shown in silver.



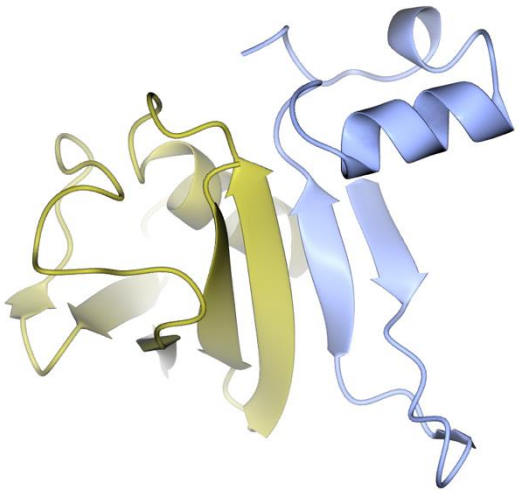
Supplemental Figure 8: Alphafold model of the tetrameric ICP0 CTD compared to the solved structure. The Alphafold model of the ICP0 CTD tetramer is shown in ribbons on the left (**A and C**), while the crystal structure is shown on the right (**B and D**), colored by the chain. The dimeric interface, particularly the twisted β-strands, were modeled accurately (**A and B**). However, generally none of the strands comprising the stacked barrels were modeled (**C and D**).



Supplemental Figure 9: Confidence of the Alphafold model of the tetrameric ICP0 CTD. The Alphafold model of the ICP0 CTD is shown in ribbons, colored by the pLDDT (confidence): confident (cyan, 90 > pLDDT > 70), low (yellow, 70 > pLDDT > 50), and very low (orange, pLDDT < 50).



Supplemental Figure 10: A model of SUMO binding anti-parallel to ICP0 at SLS5. A folded subdomain containing SLS5 is shown in silver ribbons, while SUMO is represented by gold ribbons.



Supplemental Figure 11: A model of SUMO binding parallel to ICP0 at SLS7. A folded subdomain containing SLS7 is shown in silver ribbons, while SUMO is represented by gold ribbons.

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