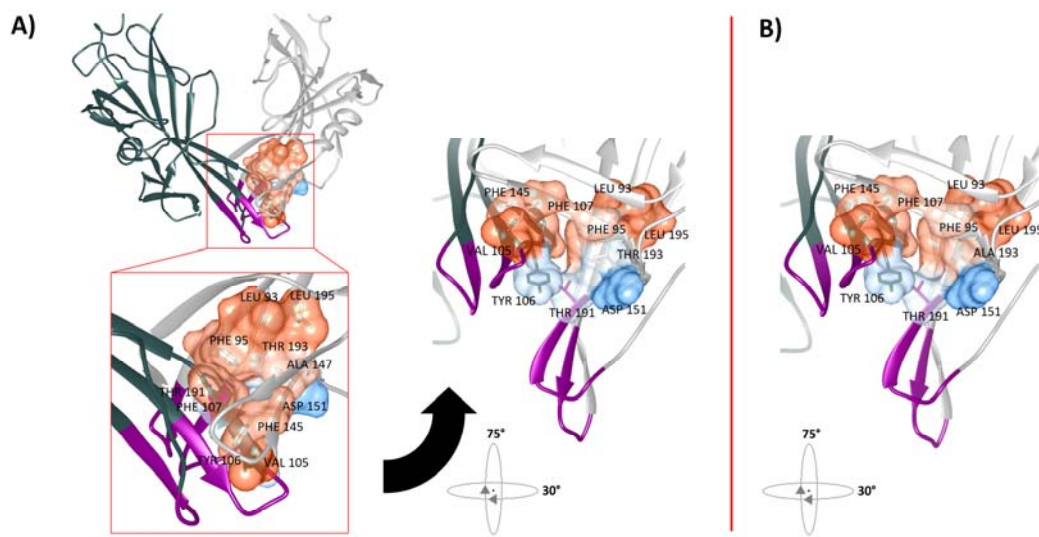


Supplement figures Tweedy et al 2017.

HHV6A	38	FRICSIAGKTDLMRFDRDISCSPYKS-NAKMSEGGFFIIYKTNIEITYTFPVRTYKKELTFO	96
HCMV	91	+R+CS+A+GTDL+RF+R+I C+ K N + EG ++YK NI +TF VR Y+K LTF+ YRVCMSAQGTDLIRFERNIVCTSMKPINEDLDEGIMVVYKRNIVAHTFKVRVYQKVLTFR	150
HHV6A	97	<b>FL1</b> SSYRDVGVVYFLDRVTMGLAMPVYEANLVNSHAQCYSAVAMKRPDGTVFSAFHEDNNKNN	156
HCMV	151	SY + Y L +A P++E + +NSH+QCYS+ + GTVF A+H D+ +N RSYAYIHTTTLGNSNTEYVAPPMEIHHINSHSQCYSSYSR-VIAGTVFVAYHRDSYENK	209
HHV6A	157	<b>FL2 Thr193Ala</b> TLNLFPLNFKSITNKRFITTKPEYFARGPLWLYSTSTSLNCIVTEATAKAKYPFSYFALT	216
HCMV	210	T+ L P ++ + + R++T K+ + +RG WLY + +LNC+VT TA++KYP+ +FA + TMQLMPDDYSNTHSTRYVTVKQWHSRGSTWLYRET <sup>■</sup> CNLNCMVTITTTARSKYPYHFFATS	269
HHV6A	217	TGEIVEGSPFFNGSN--GKHFAEPLKLTILENYTMIEDLMNGMGATTLVRKIAFLEKA	274
HCMV	270	TG+V+V SPF+NG+N +F E +K I NYT++ D N A R +AFLE+A TGDVVDISPFYNGTNRNASYFGENADKFFIFPNYTTIVSDFG-RPNSALETHRLVAFLEA	328
HHV6A	275	DTLFSWEIKEENESVCMLKHWTTVTHGLRAETNETYHFISKELTAAAFVAPKESLNLTDPK	394
HCMV	329	D++ SW+I++E C L W +R+E ++YHF S ++TA F++ K+ +N++D DSVISWDIQDEKNVTCQLTFWEASERTIRSEAEDSYHFSKMTATFLSKKQEVNMSDSA	388
HHV6A	395	QTCIKNEFEKI INEVYMSDYNDTYSMNGSYQIFKTTGDLILIWQPLVQKSLMFLEQGSEK	394
HCMV	389	C+++E + +++ + YN TY G+ +F+TTG L++ WQ + QKSL+ LE+ + + LDCVRDEAINKQQIFNTSYNGTYEKYGNVSVFETTTGGLVVFQGIKQKSLVELERLANR	448
HHV6A	395	----I---R-----RRRDVGDVKSRHDILYVQLQYLYDTLKDYLINDALGNLAESWCL	439
HCMV	449	+ R + +++S H+++Y QLQ+ YDTL+ YIN AL +AE+WC+ SSLNLTHNRTKRSTGDNATHLSNMESVHNLVYAQLQFTYDTRLRGYINRALAQIAEAWCV	508
HHV6A	440	DQKRTITMLHELKSKISPSIVSEVYGRPISAGLHGDVLAISKIEVNSQSSVQLHKSMRVV	499
HCMV	509	DQ+RT+ + ELSKI+PS+I+S +Y +PI+A+ GDVL ++ C+ +NQ+SV++ + M V DQRRTLEVFKELSKINPSAILSAINKPIAARFMGDVGLASCVTINQTSVKVLRDMNVK	568
HHV6A	500	DAKGVR.SETMCYNRPLVTFVNSSTPEVVPQGLDNEILLGDHRTEECEIPSTKIFLSG	559
HCMV	569	++ G CY+RP+V F+F NS+ V GQLG DNEILLG+HRTEEC++PS KIF++G ESPG-----RCYSRPVVIFNFANSSY-VQYQQLGEDNEILLGNHRTEECQLPSLKIFIAG	622
HHV6A	560	NHAHVYTDYTHNTSTPIEDI 579	
HCMV	623	N A+ Y DY + I NSAYEYVDYLFKRMIDLSSI 642	

**Supplement figure 1.** Alignment using Clustal of HCMV strain Merlin gB ectodomain region 91-642 with HHV-6A strain U1102 gB region 38-579 showing 228/541(42%) identity and 362/541(65%) similarity (+), with Domain I, fusion domain, region 79-291 underlined, fusion loops FL1 and FL2 in bold, and passage mutation Thr193Ala shaded. Alignments by meta-method in M-Coffee ((Wallace, I. M.; O' Sullivan, O.; Higgins, D. G.; Notredame, C. M - Coffee: combining multiple sequence alignment methods with T - Coffee. Nucleic Acids Res. 2006, 34, 1692-1699).



**Supplement figure 2.** The passage mutation in HHV-6 gB increases interface hydrophobicity affecting subunit interactions. Visualization of the residues at the interface between two subunits HHV-6A gB and residues surrounding the passage mutation site Thr193Ala. Two interacting subunits are in light and dark grey (A) and (B), with fusion loops, FL1 (residues 100-105) and FL2 (residues 184-191). The lateral chains for the residues 193, 93, 95, 145, 147, 151, 191, 195, 105, 106 and 107 located in the interface or near the position 193 were displayed (The residues 193, 93, 95, 145, 147, 151, 191 and 195 in one subunit and the residues 105, 106 and 107 in the other as visualising only one interface). The surfaces displayed correspond to their hydrophobicity (Kyte-Doolittle scale), blue hydrophilic to white at 0.0 to red hydrophobic. In (A) a global view of the interface between the Domains I of two subunits is shown (Top-left image) focusing on the subunit interfaces (Bottom left). The two other images in (A) correspond to a left-side view of the image located in bottom-left (Bottom-right image) and a top-view of the image in bottom right (Top-right image). The two images in (B) correspond to the same views with the passage substitution Thr193Ala. Stability predictions between the two HHV-6A gB subunits show a stabilizing change of the free energy value of 0.056 for a Thr193Ala mutation in one of the subunits. This contributes to the hypothesis that stabilization of subunit-subunit interactions from mutation of Thr193 to the Ala residue acts via increasing the hydrophobicity of the hydrophobic pocket (Residues 93, 95, 145, 147 and 195 surrounding 193Thr, and all conserved in HCMV as shown above). These are in Domain I where the subunits interact (at the subunits interface; residues 193, 93, 95, 145, 147, 151, 191 and 195 in one face and residues 105, 106 and 107 in the other face).

