SUPPLEMENTAL DATA

Crystal Structure of the Human Cytomegalovirus pUL50-pUL53 Core Nuclear Egress Complex Provides Insight into a Unique Assembly Scaffold for Virus-Host Protein Interactions

Sascha A. Walzer[‡], Claudia Egerer-Sieber[‡], Heinrich Sticht[§], Madhumati Sevvana[‡], Katharina Hohl[‡], Jens Milbradt[¶], Yves A. Muller[‡1,2] and Manfred Marschall[¶1,2]

From the [‡]Division of Biotechnology, Department of Biology, [§]Division of Bioinformatics, Institute of Biochemistry, [¶]Institute for Clinical and Molecular Virology[3], Friedrich-Alexander University Erlangen-Nürnberg, Germany

Running title–Crystal Structure of the HCMV Core Nuclear Egress Complex

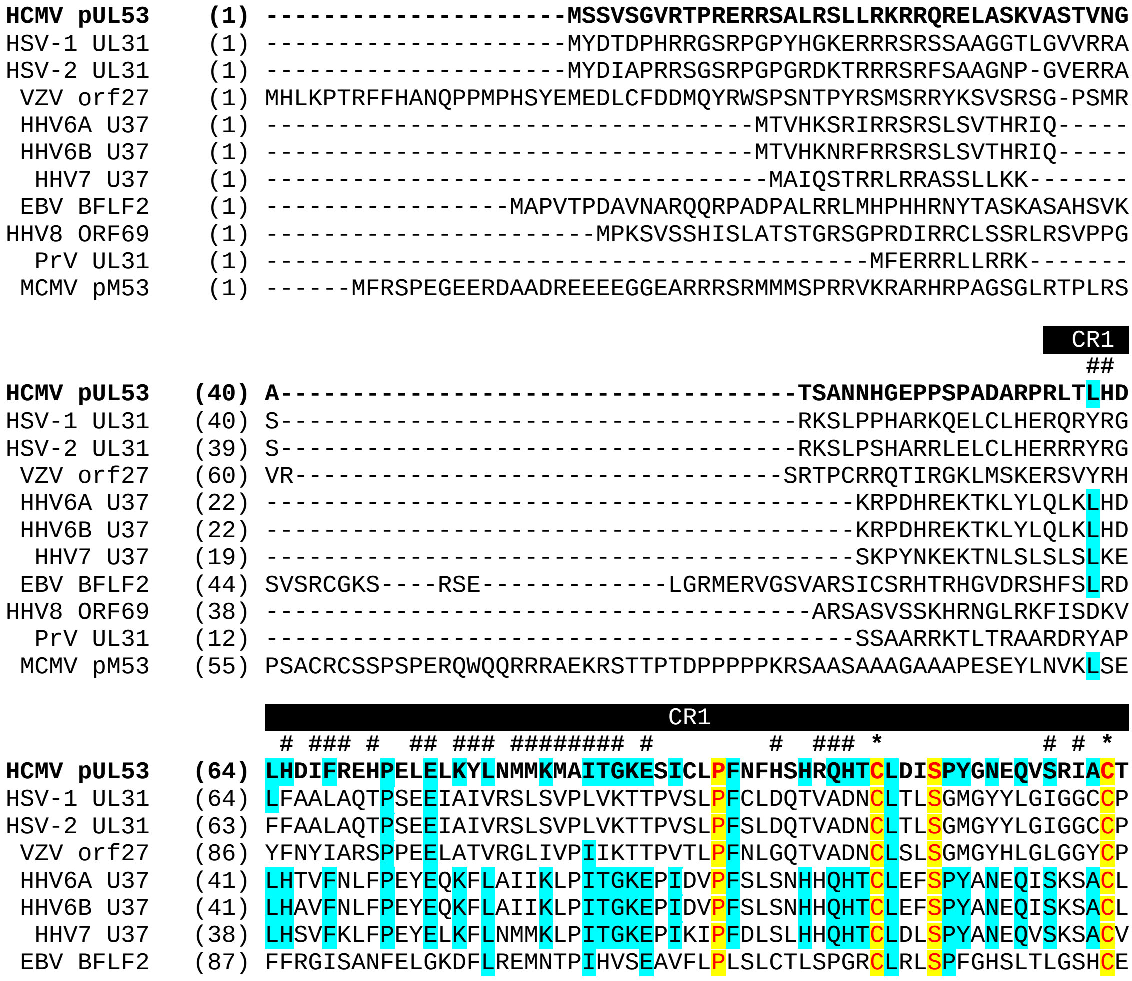
[1] Both authors contributed equally to this work.

[2] To whom correspondence should be addressed: Yves Muller, Tel.: 49-0-9131-8523082, E-mail: yves.muller@fau.de; Manfred Marschall, Tel.: 49-0-9131-8526089, E-mail: manfred.marschall@viro.med.uni-erlangen.de

SUPPLEMENTAL FIGURE 1

A

Homologs of HCMV pUL53



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HCMV pUL53     (1) ---------------------MSSVSGVRTPRERRSALRSLLRKRRQRELASKVASTVNG
HSV-1 UL31     (1) ---------------------MYDTDPHRRGSRPGPYHGKERRRSRSSAAGGTLGVVRRA
HSV-2 UL31     (1) ---------------------MYDIAPRRSGSRPGPGRDKTRRRSRFSAAGNP-GVERRA
 VZV orf27     (1) MHLKPTRFFHANQPPMPHSYEMEDLCFDDMQYRWSPSNTPYRSMSRRYKSVSRSG-PSMR
 HHV6A U37     (1) ----------------------------------MTVHKSRIRRSRSLSVTHRIQ-----
 HHV6B U37     (1) ----------------------------------MTVHKNRFRRSRSLSVTHRIQ-----
  HHV7 U37     (1) -----------------------------------MAIQSTRRLRRASSLLKK-------
 EBV BFLF2     (1) -----------------MAPVTPDAVNARQQRPADPALRRLMHPHHRNYTASKASAHSVK
HHV8 ORF69     (1) -----------------------MPKSVSSHISLATSTGRSGPRDIRRCLSSRLRSVPPG
  PrV UL31     (1) ------------------------------------------MFERRRLLRRK-------
 MCMV pM53     (1) ------MFRSPEGEERDAADREEEEGGEARRRSRMMMSPRRVKRARHRPAGSGLRTPLRS

                                                                          CR1
                                                                           ##
HCMV pUL53    (40) A------------------------------------TSANNHGEPPSPADARPRLTLHD
HSV-1 UL31    (40) S------------------------------------RKSLPPHARKQELCLHERQRYRG
HSV-2 UL31    (39) S------------------------------------RKSLPSHARRLELCLHERRRYRG
 VZV orf27    (60) VR----------------------------------SRTPCRRQTIRGKLMSKERSVYRH
 HHV6A U37    (22) -----------------------------------------KRPDHREKTKLYLQLKLHD
 HHV6B U37    (22) -----------------------------------------KRPDHREKTKLYLQLKLHD
  HHV7 U37    (19) -----------------------------------------SKPYNKEKTNLSLSLSLKE
 EBV BFLF2    (44) SVSRCGKS----RSE-------------LGRMERVGSVARSICSRHTRHGVDRSHFSLRD
HHV8 ORF69    (38) --------------------------------------ARSASVSSKHRNGLRKFISDKV
  PrV UL31    (12) -----------------------------------------SSAARRKTLTRAARDRYAP
 MCMV pM53    (55) PSACRCSSPSPERQWQQRRRAEKRSTTPTDPPPPPKRSAASAAAGAAAPESEYLNVKLSE

                                               CR1
                    # ### #  ## ### ######## #        #  ### *           # # *
HCMV pUL53    (64) LHDIFREHPELELKYLNMMKMAITGKESICLPFNFHSHRQHTCLDISPYGNEQVSRIACT
HSV-1 UL31    (64) LFAALAQTPSEEIAIVRSLSVPLVKTTPVSLPFCLDQTVADNCLTLSGMGYYLGIGGCCP
HSV-2 UL31    (63) FFAALAQTPSEEIAIVRSLSVPLVKTTPVSLPFSLDQTVADNCLTLSGMGYYLGIGGCCP
 VZV orf27    (86) YFNYIARSPPEELATVRGLIVPIIKTTPVTLPFNLGQTVADNCLSLSGMGYHLGLGGYCP
 HHV6A U37    (41) LHTVFNLFPEYEQKFLAIIKLPITGKEPIDVPFSLSNHHQHTCLEFSPYANEQISKSACL
 HHV6B U37    (41) LHAVFNLFPEYEQKFLAIIKLPITGKEPIDVPFSLSNHHQHTCLEFSPYANEQISKSACL
  HHV7 U37    (38) LHSVFKLFPEYELKFLNMMKLPITGKEPIKIPFDLSLHHQHTCLDLSPYANEQVSKSACV
 EBV BFLF2    (87) FFRGISANFELGKDFLREMNTPIHVSEAVFLPLSLCTLSPGRCLRLSPFGHSLTLGSHCE
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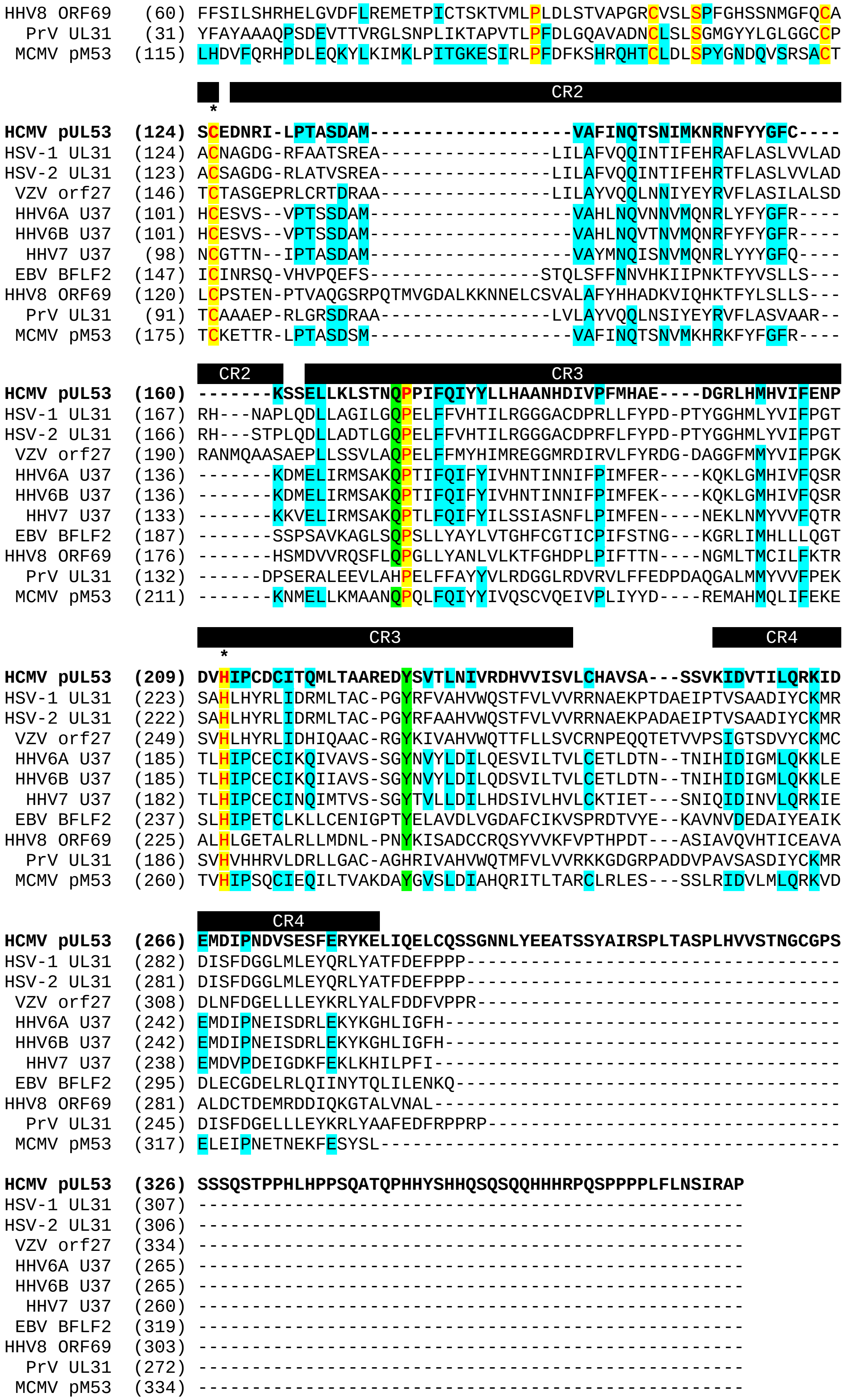

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 HHV8 ORF69   (60) FFSILSHRHELGVDFLREMETPICTSKTVMLPLDLSTVAPGRCVSLSPFGHSSNMGFQCA
   PrV UL31   (31) YFAYAAAQPSDEVTTVRGLSNPLIKTAPVTLPFDLGQAVADNCLSLSGMGYYLGLGGCCP
  MCMV pM53  (115) LHDVFQRHPDLEQKYLKIMKLPITGKESIRLPFDFKSHRQHTCLDLSPYGNDQVSRSACT

                                                    CR2
                    *
 HCMV pUL53  (124) SCEDNRI-LPTASDAM-------------------VAFINQTSNIMKNRNFYYGFC----
 HSV-1 UL31  (124) ACNAGDG-RFAATSREA----------------LILAFVQQINTIFEHRAFLASLVVLAD
 HSV-2 UL31  (123) ACSAGDG-RLATVSREA----------------LILAFVQQINTIFEHRTFLASLVVLAD
  VZV orf27  (146) TCTASGEPRLCRTDRAA----------------LILAYVQQLNNIYEYRVFLASILALSD
  HHV6A U37  (101) HCESVS--VPTSSDAM-------------------VAHLNQVNNVMQNRLYFYGFR----
  HHV6B U37  (101) HCESVS--VPTSSDAM-------------------VAHLNQVTNVMQNRFYFYGFR----
   HHV7 U37   (98) NCGTTN--IPTASDAM-------------------VAYMNQISNVMQNRLYYYGFQ----
  EBV BFLF2  (147) ICINRSQ-VHVPQEFS----------------STQLSFFNNVHKIIPNKTFYVSLLS---
 HHV8 ORF69  (120) LCPSTEN-PTVAQGSRPQTMVGDALKKNNELCSVALAFYHHADKVIQHKTFYLSLLS---
   PrV UL31   (91) TCAAAEP-RLGRSDRAA----------------LVLAYVQQLNSIYEYRVFLASVAAR--
  MCMV pM53  (175) TCKETTR-LPTASDSM-------------------VAFINQTSNVMKHRKFYFGFR----

                     CR2                            CR3
 HCMV pUL53  (160) -------KSSELLKLSTNQPPIFQIYYLLHAANHDIVPFMHAE----DGRLHMHVIFENP
 HSV-1 UL31  (167) RH---NAPLQDLLAGILGQPELFFVHTILRGGGACDPRLLFYPD-PTYGGHMLYVIFPGT
 HSV-2 UL31  (166) RH---STPLQDLLADTLGQPELFFVHTILRGGGACDPRFLFYPD-PTYGGHMLYVIFPGT
  VZV orf27  (190) RANMQAASAEPLLSSVLAQPELFFMYHIMREGGMRDIRVLFYRDG-DAGGFMMYVIFPGK
  HHV6A U37  (136) -------KDMELIRMSAKQPTIFQIFYIVHNTINNIFPIMFER----KQKLGMHIVFQSR
  HHV6B U37  (136) -------KDMELIRMSAKQPTIFQIFYIVHNTINNIFPIMFEK----KQKLGMHIVFQSR
   HHV7 U37  (133) -------KKVELIRMSAKQPTLFQIFYILSSIASNFLPIMFEN----NEKLNMYVVFQTR
  EBV BFLF2  (187) -------SSPSAVKAGLSQPSLLYAYLVTGHFCGTICPIFSTNG---KGRLIMHLLLQGT
 HHV8 ORF69  (176) -------HSMDVVRQSFLQPGLLYANLVLKTFGHDPLPIFTTN----NGMLTMCILFKTR
   PrV UL31  (132) ------DPSERALEEVLAHPELFFAYYVLRDGGLRDVRVLFFEDPDAQGALMMYVVFPEK
  MCMV pM53  (211) -------KNMELLKMAANQPQLFQIYYIVQSCVQEIVPLIYYD----REMAHMQLIFEKE

                                    CR3                                CR4
                     *
 HCMV pUL53  (209) DVHIPCDCITQMLTAAREDYSVTLNIVRDHVVISVLCHAVSA---SSVKIDVTILQRKID
 HSV-1 UL31  (223) SAHLHYRLIDRMLTAC-PGYRFVAHVWQSTFVLVVRRNAEKPTDAEIPTVSAADIYCKMR
 HSV-2 UL31  (222) SAHLHYRLIDRMLTAC-PGYRFAAHVWQSTFVLVVRRNAEKPADAEIPTVSAADIYCKMR
  VZV orf27  (249) SVHLHYRLIDHIQAAC-RGYKIVAHVWQTTFLLSVCRNPEQQTETVVPSIGTSDVYCKMC
  HHV6A U37  (185) TLHIPCECIKQIVAVS-SGYNVYLDILQESVILTVLCETLDTN--TNIHIDIGMLQKKLE
  HHV6B U37  (185) TLHIPCECIKQIIAVS-SGYNVYLDILQDSVILTVLCETLDTN--TNIHIDIGMLQKKLE
   HHV7 U37  (182) TLHIPCECINQIMTVS-SGYTVLLDILHDSIVLHVLCKTIET---SNIQIDINVLQRKIE
  EBV BFLF2  (237) SLHIPETCLKLLCENIGPTYELAVDLVGDAFCIKVSPRDTVYE--KAVNVDEDAIYEAIK
 HHV8 ORF69  (225) ALHLGETALRLLMDNL-PNYKISADCCRQSYVVKFVPTHPDT---ASIAVQVHTICEAVA
   PrV UL31  (186) SVHVHHRVLDRLLGAC-AGHRIVAHVWQTMFVLVVRKKGDGRPADDVPAVSASDIYCKMR
  MCMV pM53  (260) TVHIPSQCIEQILTVAKDAYGVSLDIAHQRITLTARCLRLES---SSLRIDVLMLQRKVD

                           CR4
 HCMV pUL53  (266) EMDIPNDVSESFERYKELIQELCQSSGNNLYEEATSSYAIRSPLTASPLHVVSTNGCGPS
 HSV-1 UL31  (282) DISFDGGLMLEYQRLYATFDEFPPP-----------------------------------
 HSV-2 UL31  (281) DISFDGGLMLEYQRLYATFDEFPPP-----------------------------------
  VZV orf27  (308) DLNFDGELLLEYKRLYALFDDFVPPR----------------------------------
  HHV6A U37  (242) EMDIPNEISDRLEKYKGHLIGFH-------------------------------------
  HHV6B U37  (242) EMDIPNEISDRLEKYKGHLIGFH-------------------------------------
   HHV7 U37  (238) EMDVPDEIGDKFEKLKHILPFI--------------------------------------
  EBV BFLF2  (295) DLECGDELRLQIINYTQLILENKQ------------------------------------
 HHV8 ORF69  (281) ALDCTDEMRDDIQKGTALVNAL--------------------------------------
   PrV UL31  (245) DISFDGELLLEYKRLYAAFEDFRPPRP---------------------------------
  MCMV pM53  (317) ELEIPNETNEKFESYSL-------------------------------------------

 HCMV pUL53  (326) SSSQSTPPHLHPPSQATQPHHYSHHQSQSQQHHHRPQSPPPPLFLNSIRAP
 HSV-1 UL31  (307) ---------------------------------------------------
 HSV-2 UL31  (306) ---------------------------------------------------
  VZV orf27  (334) ---------------------------------------------------
  HHV6A U37  (265) ---------------------------------------------------
  HHV6B U37  (265) ---------------------------------------------------
   HHV7 U37  (260) ---------------------------------------------------
  EBV BFLF2  (319) ---------------------------------------------------
 HHV8 ORF69  (303) ---------------------------------------------------
   PrV UL31  (272) ---------------------------------------------------
  MCMV pM53  (334) ---------------------------------------------------
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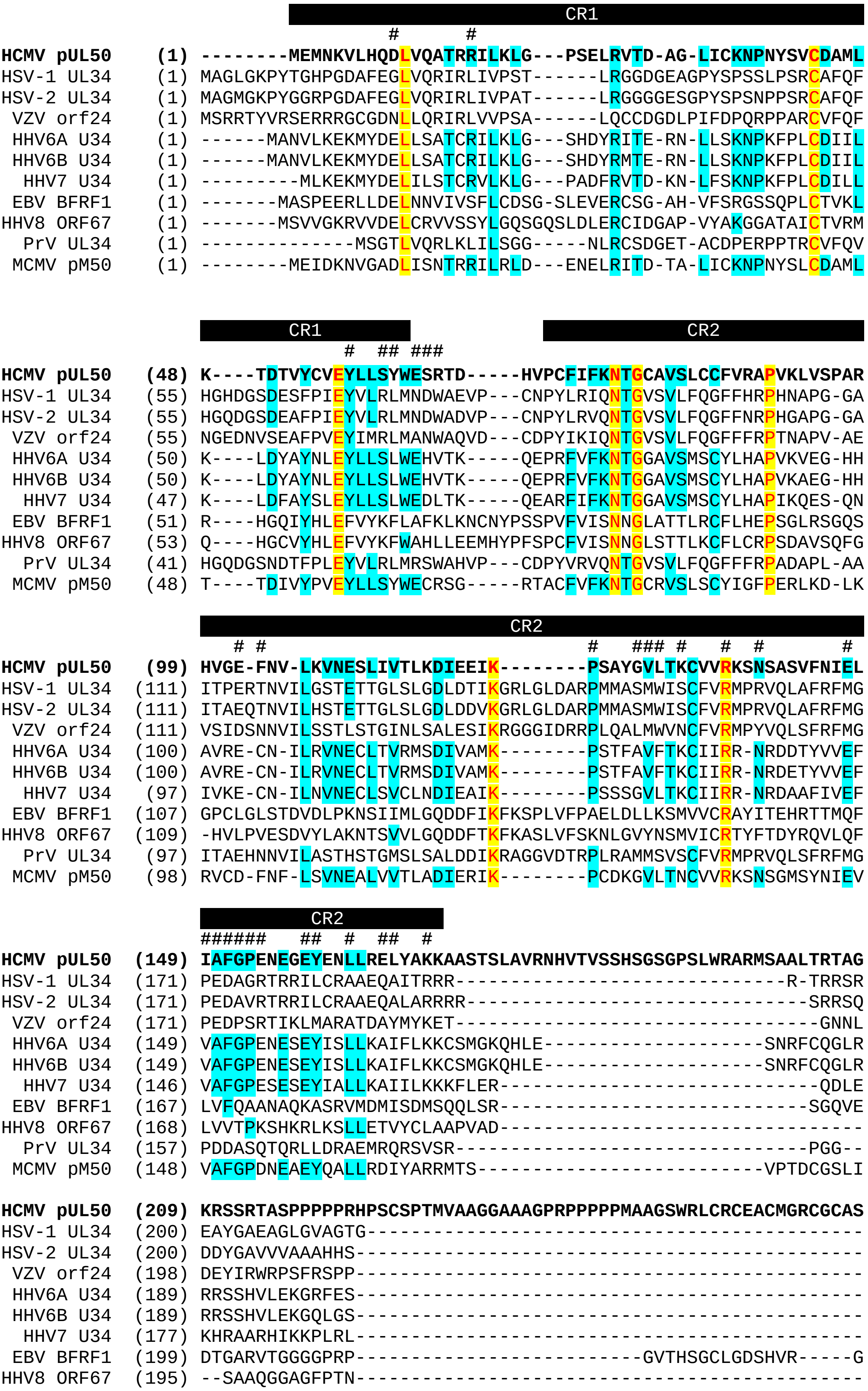
B

Homologs of HCMV pUL50



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                                                    CR1
                                    #      #
HCMV pUL50     (1) --------MEMNKVLHQDLVQATRRILKLG---PSELRVTD-AG-LICKNPNYSVCDAML
HSV-1 UL34     (1) MAGLGKPYTGHPGDAFEGLVQRIRLIVPST------LRGGDGEAGPYSPSSLPSRCAFQF
HSV-2 UL34     (1) MAGMGKPYGGRPGDAFEGLVQRIRLIVPAT------LRGGGGESGPYSPSNPPSRCAFQF
 VZV orf24     (1) MSRRTYVRSERRRGCGDNLLQRIRLVVPSA------LQCCDGDLPIFDPQRPPARCVFQF
 HHV6A U34     (1) ------MANVLKEKMYDELLSATCRILKLG---SHDYRITE-RN-LLSKNPKFPLCDIIL
 HHV6B U34     (1) ------MANVLKEKMYDELLSATCRILKLG---SHDYRMTE-RN-LLSKNPKFPLCDIIL
  HHV7 U34     (1) ---------MLKEKMYDELILSTCRVLKLG---PADFRVTD-KN-LFSKNPKFPLCDILL
 EBV BFRF1     (1) -------MASPEERLLDELNNVIVSFLCDSG-SLEVERCSG-AH-VFSRGSSQPLCTVKL
HHV8 ORF67     (1) -------MSVVGKRVVDELCRVVSSYLGQSGQSLDLERCIDGAP-VYAKGGATAICTVRM
  PrV UL34     (1) --------------MSGTLVQRLKLILSGG-----NLRCSDGET-ACDPERPPTRCVFQV
 MCMV pM50     (1) --------MEIDKNVGADLISNTRRILRLD---ENELRITD-TA-LICKNPNYSLCDAML

                           CR1                                 CR2
                                #  ## ###
HCMV pUL50    (48) K----TDTVYCVEYLLSYWESRTD-----HVPCFIFKNTGCAVSLCCFVRAPVKLVSPAR
HSV-1 UL34    (55) HGHDGSDESFPIEYVLRLMNDWAEVP---CNPYLRIQNTGVSVLFQGFFHRPHNAPG-GA
HSV-2 UL34    (55) HGQDGSDEAFPIEYVLRLMNDWADVP---CNPYLRVQNTGVSVLFQGFFNRPHGAPG-GA
 VZV orf24    (55) NGEDNVSEAFPVEYIMRLMANWAQVD---CDPYIKIQNTGVSVLFQGFFFRPTNAPV-AE
 HHV6A U34    (50) K----LDYAYNLEYLLSLWEHVTK-----QEPRFVFKNTGGAVSMSCYLHAPVKVEG-HH
 HHV6B U34    (50) K----LDYAYNLEYLLSLWEHVTK-----QEPRFVFKNTGGAVSMSCYLHAPVKAEG-HH
  HHV7 U34    (47) K----LDFAYSLEYLLSLWEDLTK-----QEARFIFKNTGGAVSMSCYLHAPIKQES-QN
 EBV BFRF1    (51) R----HGQIYHLEFVYKFLAFKLKNCNYPSSPVFVISNNGLATTLRCFLHEPSGLRSGQS
HHV8 ORF67    (53) Q----HGCVYHLEFVYKFWAHLLEEMHYPFSPCFVISNNGLSTTLKCFLCRPSDAVSQFG
  PrV UL34    (41) HGQDGSNDTFPLEYVLRLMRSWAHVP---CDPYVRVQNTGVSVLFQGFFFRPADAPL-AA
 MCMV pM50    (48) T----TDIVYPVEYLLSYWECRSG-----RTACFVFKNTGCRVSLSCYIGFPERLKD-LK

                                                CR2
                      # #                             #   ### #   #  #       #
HCMV pUL50    (99) HVGE-FNV-LKVNESLIVTLKDIEEIK--------PSAYGVLTKCVVRKSNSASVFNIEL
HSV-1 UL34   (111) ITPERTNVILGSTETTGLSLGDLDTIKGRLGLDARPMMASMWISCFVRMPRVQLAFRFMG
HSV-2 UL34   (111) ITAEQTNVILHSTETTGLSLGDLDDVKGRLGLDARPMMASMWISCFVRMPRVQLAFRFMG
 VZV orf24   (111) VSIDSNNVILSSTLSTGINLSALESIKRGGGIDRRPLQALMWVNCFVRMPYVQLSFRFMG
 HHV6A U34   (100) AVRE-CN-ILRVNECLTVRMSDIVAMK--------PSTFAVFTKCIIRR-NRDDTYVVEF
 HHV6B U34   (100) AVRE-CN-ILRVNECLTVRMSDIVAMK--------PSTFAVFTKCIIRR-NRDETYVVEF
  HHV7 U34    (97) IVKE-CN-ILNVNECLSVCLNDIEAIK--------PSSSGVLTKCIIRR-NRDAAFIVEF
 EBV BFRF1   (107) GPCLGLSTDVDLPKNSIIMLGQDDFIKFKSPLVFPAELDLLKSMVVCRAYITEHRTTMQF
HHV8 ORF67   (109) -HVLPVESDVYLAKNTSVVLGQDDFTKFKASLVFSKNLGVYNSMVICRTYFTDYRQVLQF
  PrV UL34    (97) ITAEHNNVILASTHSTGMSLSALDDIKRAGGVDTRPLRAMMSVSCFVRMPRVQLSFRFMG
 MCMV pM50    (98) RVCD-FNF-LSVNEALVVTLADIERIK--------PCDKGVLTNCVVRKSNSGMSYNIEV

                             CR2
                   ######   ##  #  ##  #
HCMV pUL50   (149) IAFGPENEGEYENLLRELYAKKAASTSLAVRNHVTVSSHSGSGPSLWRARMSAALTRTAG
HSV-1 UL34   (171) PEDAGRTRRILCRAAEQAITRRR------------------------------R-TRRSR
HSV-2 UL34   (171) PEDAVRTRRILCRAAEQALARRRR-------------------------------SRRSQ
 VZV orf24   (171) PEDPSRTIKLMARATDAYMYKET---------------------------------GNNL
 HHV6A U34   (149) VAFGPENESEYISLLKAIFLKKCSMGKQHLE--------------------SNRFCQGLR
 HHV6B U34   (149) VAFGPENESEYISLLKAIFLKKCSMGKQHLE--------------------SNRFCQGLR
  HHV7 U34   (146) VAFGPESESEYIALLKAIILKKKFLER-----------------------------QDLE
 EBV BFRF1   (167) LVFQAANAQKASRVMDMISDMSQQLSR----------------------------SGQVE
HHV8 ORF67   (168) LVVTPKSHKRLKSLLETVYCLAAPVAD---------------------------------
  PrV UL34   (157) PDDASQTQRLLDRAEMRQRSVSR--------------------------------PGG--
 MCMV pM50   (148) VAFGPDNEAEYQALLRDIYARRMTS--------------------------VPTDCGSLI

HCMV pUL50   (209) KRSSRTASPPPPPRHPSCSPTMVAAGGAAAGPRPPPPPMAAGSWRLCRCEACMGRCGCAS
HSV-1 UL34   (200) EAYGAEAGLGVAGTG---------------------------------------------
HSV-2 UL34   (200) DDYGAVVVAAAHHS----------------------------------------------
 VZV orf24   (198) DEYIRWRPSFRSPP----------------------------------------------
 HHV6A U34   (189) RRSSHVLEKGRFES----------------------------------------------
 HHV6B U34   (189) RRSSHVLEKGQLGS----------------------------------------------
  HHV7 U34   (177) KHRAARHIKKPLRL----------------------------------------------
 EBV BFRF1   (199) DTGARVTGGGGPRP--------------------------GVTHSGCLGDSHVR-----G
HHV8 ORF67   (195) --SAAQGGAGFPTN----------------------------------------------
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  PrV UL34  (183) GAGGGDDGEGPSPR----------------------------------------------
 MCMV pM50  (182) CRRARCLAAAPPRR-------------------PPPPPPPGQRWGSLRKHGPVLTRRYAG

HCMV pUL50  (269) EGDADEEEEELLALAGEGKAAAAAAGQDVGGSARRPLEEHVSRRRGVSTHHRHPPSPPCA
HSV-1 UL34  (215) -------------------FRARGDGFGPLPLLTQGPSR---------------------
HSV-2 UL34  (214) -------------------SGAPGPGVAASGPPAPPGRG---------------------
 VZV orf24  (212) ------------------ENGSPNTSVQMQSDIKPA------------------------
 HHV6A U34  (203) ------SGK------VVNKASAVVTSQESIKQFYEK-------------------EK---
 HHV6B U34  (203) ------SGE------IANKASAVVTSQESINQFYEK-------------------EK---
  HHV7 U34  (191) ----------------QLKSVGEMTSFRSINYMGNT-------------------KD---
 EBV BFRF1  (228) RGG---WDLDNFSEAETEDEASYAPWRDKDSWSESE-------------------AAPWK
HHV8 ORF67  (207) ----------------GRDARACTSDVTAVYWAGQG------------------------
  PrV UL34  (197) -------------APIRPTVISPVPGHAAAAFVGQAAYP---------------------
 MCMV pM50  (223) GGGAAKNQPAAASPTSTSTSSPAAPSRDQDQTQRPP------------------PAGDTN

HCMV pUL50  (329) PSLERTGYRWAPSSWWRARSGPSRPQSGPWLPARFATLGPLVLALLLVLALLWRGHGQSS
HSV-1 UL34  (235) ------PWHQALRGLKHLRIG------------PPALVLAAGLVLGAAIWWVVGAGARL-
HSV-2 UL34  (234) ---PARPWHQAVQLFRAPRPG-----------PPALLLLAAGLFLGAAIWWAVGARL---
 VZV orf24  (230) -----LPDTQTTRVWKLALPVAN-------VTYALFIVIVLVVVLGAVLFWK--------
 HHV6A U34  (229) -------SLLSGVKFWRLSER----------HCRFALVGICFLLALYFCYVLLKKTPTPA
 HHV6B U34  (229) -------SFLSGVKFSRLSER----------HCRVAIVSICFLLALYFCYVLLKKTPTPA
  HHV7 U34  (213) -----AAVFPVTVPIFARRNN--------------ILCGFLVAALLIVCYVIFKEFALSA
 EBV BFRF1  (266) KELVRHPIRRHRTRETRRMRGSHSRVEHVPPETRETVVGGAWRYSWRATPYLARVLAVTA
HHV8 ORF67  (227) -------------GRTVRILG-----------AFQWSLGRAVALVRRSWPWISAGIAFLC
  PrV UL34  (223) ------PPARFPASLLHTLLG-----------LR-RLAGYAVACVTGALAIVIILNMR--
 MCMV pM50  (265) VTAAETTYSERTISFLTRHAN----------AIHCALILAAAIALVLLWLLYWHAARSAG

HCMV pUL50  (389) SPTRSAHRD--
HSV-1 UL34  (276) -----------
HSV-2 UL34  (277) -----------
 VZV orf24  (270) -----------
 HHV6A U34  (272) SGSVV------
 HHV6B U34  (272) SGPVV------
  HHV7 U34  (254) DFSAV------
 EBV BFRF1  (326) VALLLMFLRWT
HHV8 ORF67  (263) LGLVWMRPS--
  PrV UL34  (263) -----------
 MCMV pM50  (315) HP---------
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SUPPLEMENTAL FIGURE 1. **Protein sequence alignment of pUL50 and pUL53 homologs.** Using the ClustalW algorithm (33) by AlignX (component of Vector NTI Advance 9.1.0; Invitrogen), multiple alignments of the full amino acid sequences of pUL53 (A) and pUL50 (B) homologs of human herpesviruses (herpes simplex virus types 1 and 2, HSV-1/-2; varicella zoster virus, VZV; human cytomegalovirus, HCMV; human herpesvirus 6 variants A and B, HHV-6A/B; human herpesvirus 7, HHV-7; Epstein-Barr virus, EBV; and human herpesvirus 8, HHV-8/KSHV) and animal herpesviruses (pseudorabies virus, PrV and murine cytomegalovirus, MCMV) were performed. The sequences were selected from the UniProt Knowledgebase (http://www.uniprot.org/):

pUL53 homologs – UL31 of HSV-1 strain 17 (accession number P10215), UL31 of HSV-2 strain HG52 (P89454), ORF27 of VZV strain Dumas (P09283), pUL53 of HCMV strain AD169 (P16794), U37 of HHV-6A strain Uganda (P28865), U37 of HHV-6B strain HST (Q9WT27), U37 of HHV-7 strain JI (P52361), BFLF2 of EBV strain B95-8 (P0CK47), ORF67 of HHV-8 strain GK18 (F5H982), UL34 of PrV strain Kaplan (Q911V7), and pM53 of MCMV (H2A291).

pUL50 homologs – UL34 of HSV-1 strain 17 (P10218), UL34 of HSV-2 strain HG52 (P89457), ORF24 of VZV strain Dumas (P09280), pUL50 of HCMV strain AD169 (P16791), U34 of HHV-6A strain Uganda (P52465), U34 of HHV-6B strain Z29 (Q9QJ35), U34 of HHV-7 strain JI (P52466), BFRF1 of EBV strain B95–8 (P03185), ORF67 of HHV-8 strain GK18 (Q76RF3), UL34 of PrV strain Kaplan (Q9ICS7), and pM50 of MCMV (H2A365).

Alignment coloring scheme: red on yellow, identical residues throughout all analyzed sequences; black on green, identical residues in all sequences of human herpesviruses; black on cyan, identical residues in all sequences of betaherpesviruses (HCMV, HHV-6A/B, HHV-7, and MCMV). The previously identified conserved regions within homologs of pUL53 (CR1 to CR4) and pUL50 (CR1 and CR2) (14, 34) are depicted on top of the sequence alignments as black bars. Residues of pUL50 and pUL53 which interact with the respective binding partner are marked by #; residues of pUL53 which constitute a zinc finger are marked by *. Note, that almost all residues of the interaction surface are located within the conserved regions (pUL53, CR1; pUL50, CR1 and CR2) and that the residues of the zinc finger (Cys106, Cys122, Cys125, His211) are strictly conserved among homologous sequences of pUL53.