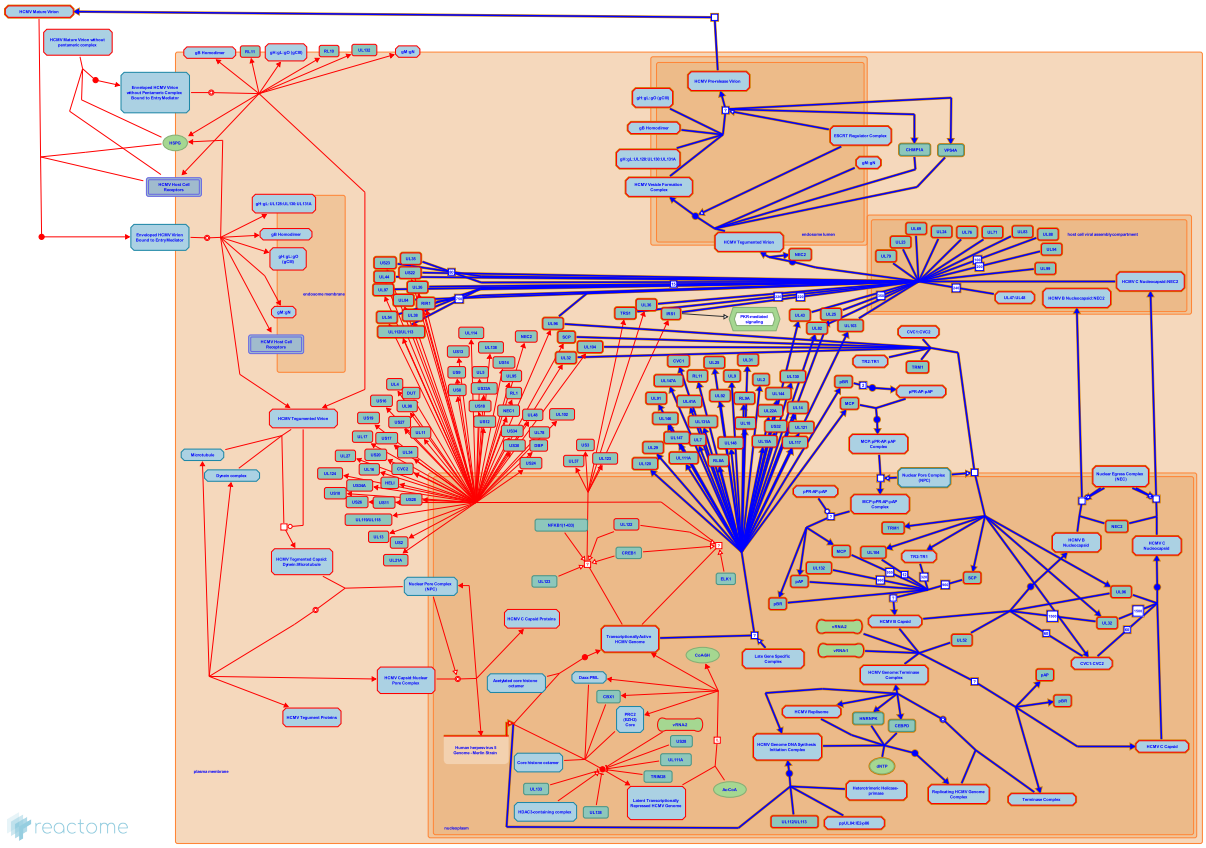
HCMV Late Events



Caposio, P., Gillespie, ME., Guerreiro, C., Streblow, DN.

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28/04/2024

Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.
The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

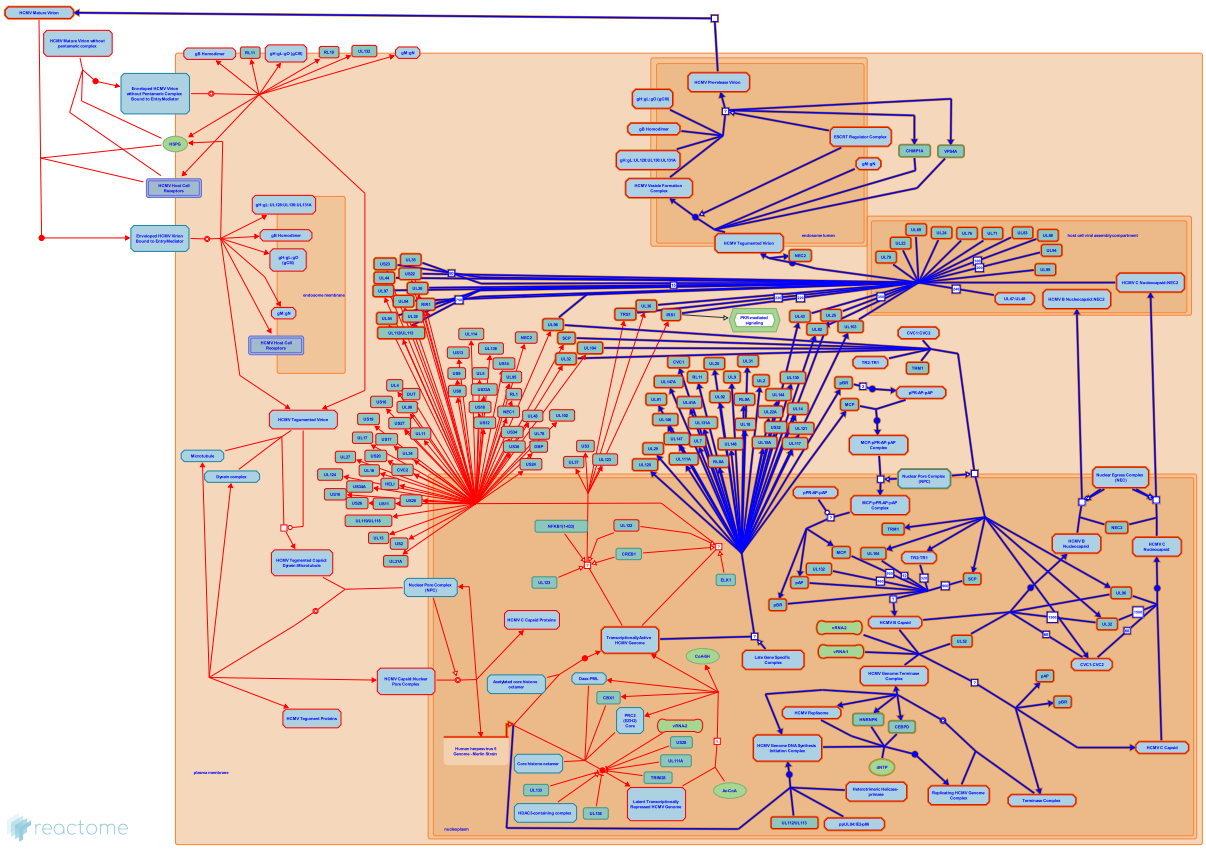
Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

HCMV Late Events ↗

Stable identifier: R-HSA-9610379

Diseases: viral infectious disease



Once Human Cytomegalovirus (HCMV) Immediate Early (IE) and Delayed Early (DE) gene products begin to appear the processes driving DNA replication, Late (L) gene expression, and virion assembly begin.

Literature references

von König, CH., Drosten, C., Blümel, J., Schlenkrich, U., Heiden, M., Burger, R. et al. (2010). Human Cytomegalovirus (HCMV) - Revised. *Transfus Med Hemother, 37*, 365-375. ↗

Cristea, IM., Jean Beltran, PM. (2014). The life cycle and pathogenesis of human cytomegalovirus infection: lessons from proteomics. *Expert Rev Proteomics, 11*, 697-711. ↗

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins.*

Aicheler, R., Stanton, RJ., Wilkie, GS., Weekes, M., Murrell, I., Davison, AJ. et al. (2015). Human cytomegalovirus: taking the strain. *Med. Microbiol. Immunol., 204*, 273-84. ↗

Editions

2018-05-26	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Initiation of HCMV DNA Replication ↗

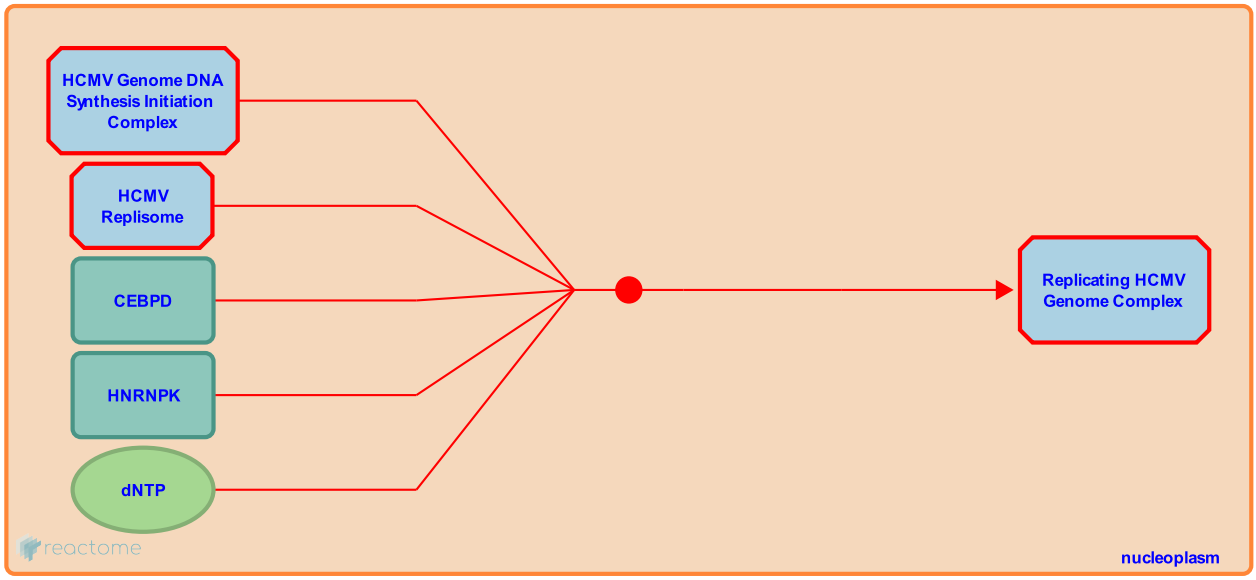
Location: HCMV Late Events

Stable identifier: R-HSA-9624033

Type: binding

Compartments: nucleoplasm

Diseases: disease by infectious agent



DNA synthesis occurs in the nucleus and relies on a core set of virus-coded proteins composed of replication fork machinery that work together to promote replication initiation on the oriLyt region. DNA synthesis initiates in the vicinity of oriLyt as soon as essential virus encoded proteins appear, producing high molecular weight replication intermediates. Onset of viral DNA synthesis licenses transcription of a subset of the late class (L) of viral genes, many of which encode proteins that take part in virion assembly.

Followed by: Assembly of the HCMV Genome DNA Replication Complex

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-10-03	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Assembly of the HCMV Genome DNA Replication Complex ↗

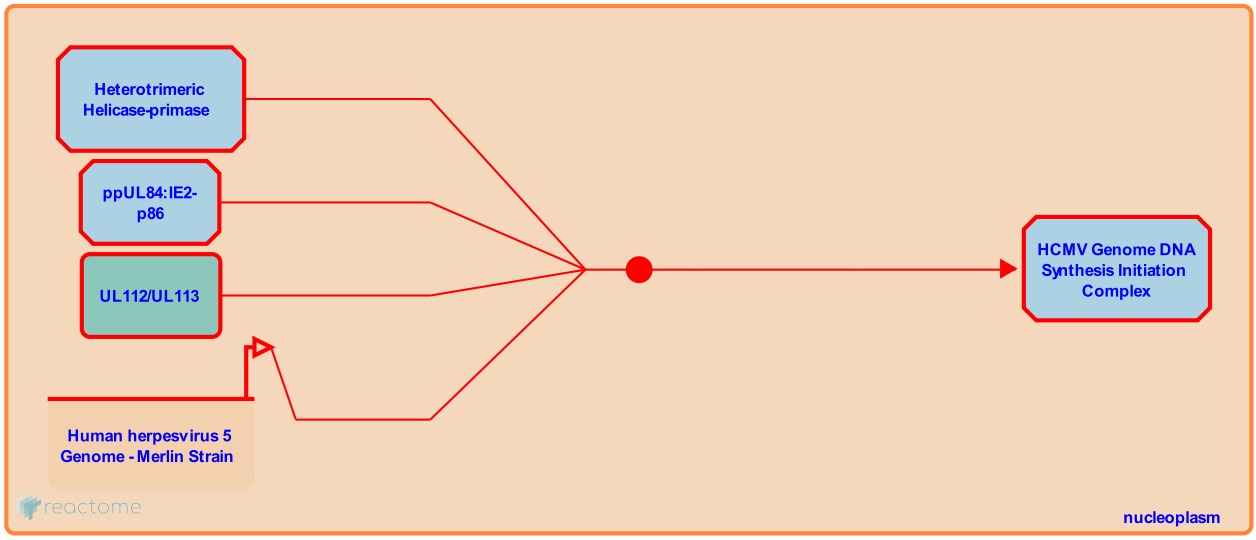
Location: HCMV Late Events

Stable identifier: R-HSA-9698927

Type: binding

Compartments: nucleoplasm

Diseases: disease by infectious agent



During late stages of Human Cytomegalovirus (HCMV) infection viral DNA replication is established. Viral Proteins, UL36, UL49, UL80, UL100, UL117, UL112-UL113, and TRS1 all play a role in DNA replication. UL76 was found to modulate the expression of the essential protein UL77 possibly as part of a mechanism to modulate UL77 levels required for efficient viral replication. Furthermore UL55 and UL76 were found to inhibit DNA replication suggesting that these viral factors are likely key proteins to fine-tune the replication process.

Preceded by: Initiation of HCMV DNA Replication

Followed by: HCMV Genome Replication Completion

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-10-03	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

HCMV Genome Replication Completion ↗

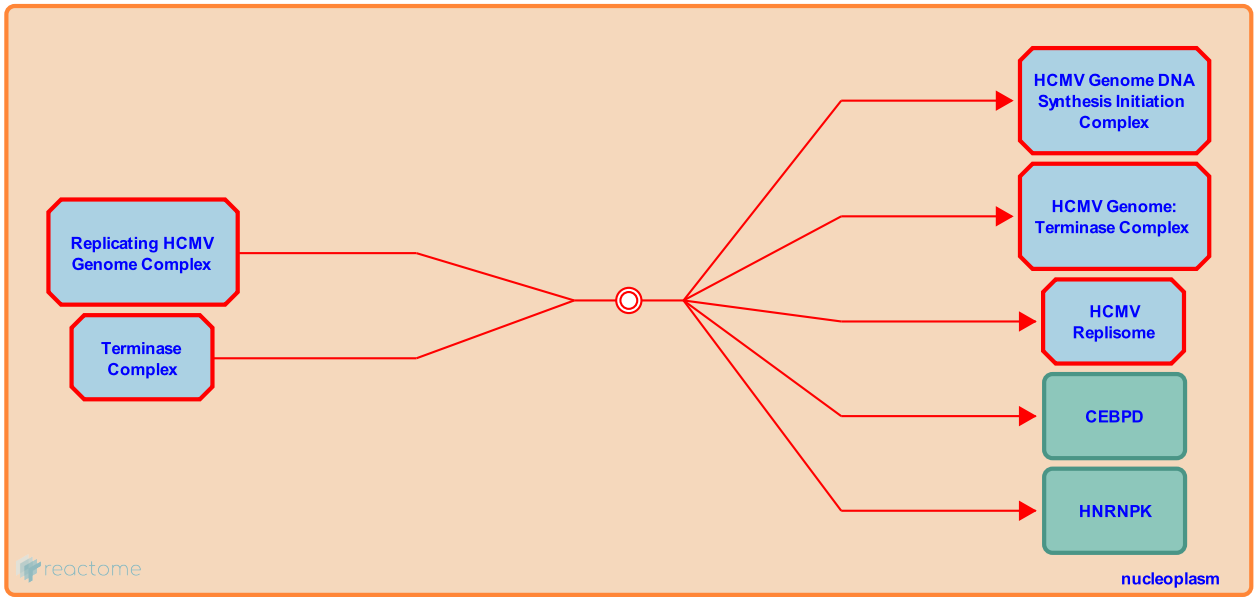
Location: HCMV Late Events

Stable identifier: R-HSA-9698926

Type: dissociation

Compartments: nucleoplasm

Diseases: viral infectious disease



Human Cytomegalovirus (HCMV) DNA synthesis may start replication using a theta form initiating at an origin and generating a replication bubble before switching to a rolling circle mode of replication. The architecture of replicating DNA is consistent with concatemeric structures generated by rolling circle form of replication, and this is the likely template for the genome encapsidation. Replication ends with the association of the Terminase complex and the threading of the completed genome into the procapsid

Preceded by: Assembly of the HCMV Genome DNA Replication Complex

Followed by: Late (L) Gene Expression

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-11-28	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Late (L) Gene Expression ↗

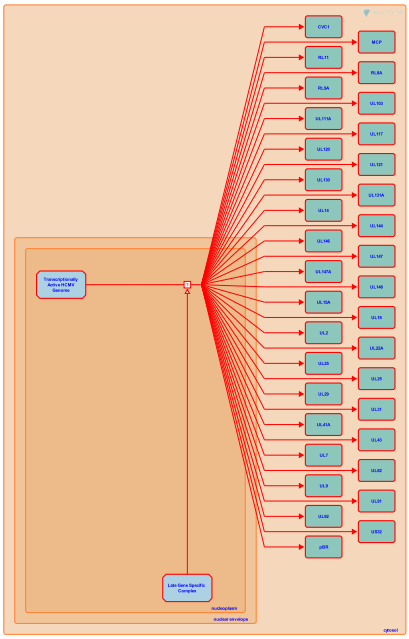
Location: HCMV Late Events

Stable identifier: R-HSA-9698928

Type: uncertain

Compartments: nucleoplasm

Diseases: disease by infectious agent



Once Human Cytomegalovirus (HCMV) viral DNA synthesis is underway transcription of a subset of the late class (L) of viral genes, many of which encode proteins that take part in virion assembly ensues.

Preceded by: HCMV Genome Replication Completion

Followed by: Binding of pPR-AP to pAP to form the pPR-AP:pAP Complex

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Binding of pPR-AP to pAP to form the pPR-AP:pAP Complex ↗

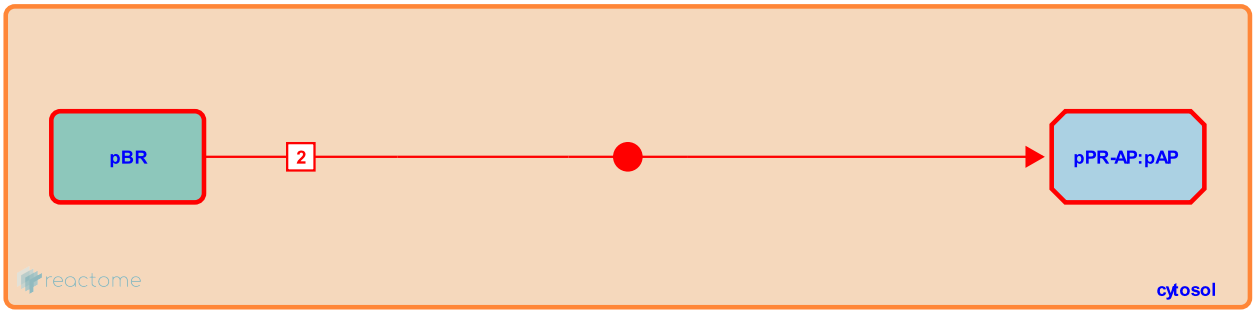
Location: HCMV Late Events

Stable identifier: R-HSA-9698962

Type: binding

Compartments: cytosol

Diseases: viral infectious disease



The process of capsid formation begins with the formation of the maturational protease precursor complex (pPR-AP:pAP).

Preceded by: Late (L) Gene Expression

Followed by: Binding of the major capsid protein (MCP) to the pPR-AP:pAP complex

Literature references

Gibson, W. (2008). Structure and formation of the cytomegalovirus virion. *Curr. Top. Microbiol. Immunol., 325*, 187-204. ↗

Binding of the major capsid protein (MCP) to the pPR-AP:pAP complex ↗

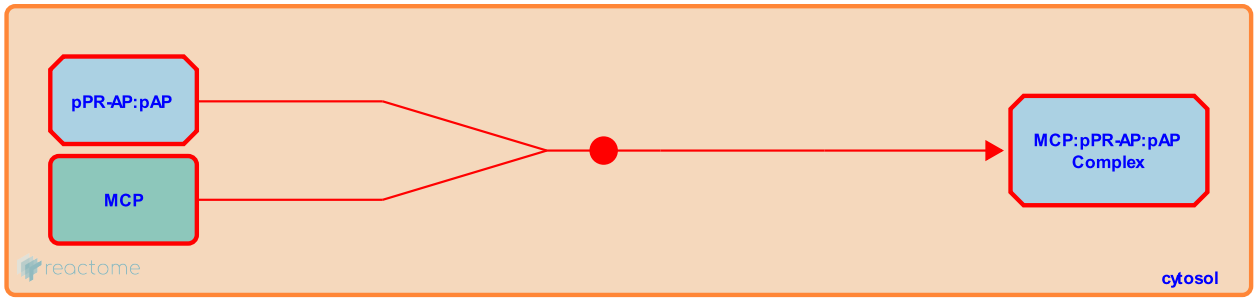
Location: HCMV Late Events

Stable identifier: R-HSA-9698923

Type: binding

Compartments: cytosol

Diseases: viral infectious disease



The process of capsid formation gets underway when the newly translated major capsid protein (MCP) associates with the maturational protease precursor complex (pPR-AP:pAP). Once the complex is formed it is transported into the nucleus.

Preceded by: Binding of pPR-AP to pAP to form the pPR-AP:pAP Complex

Followed by: Transport of MCP:pPR-AP:pAP Complex into the Nucleous

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Transport of MCP:pPR-AP:pAP Complex into the Nucleous ↗

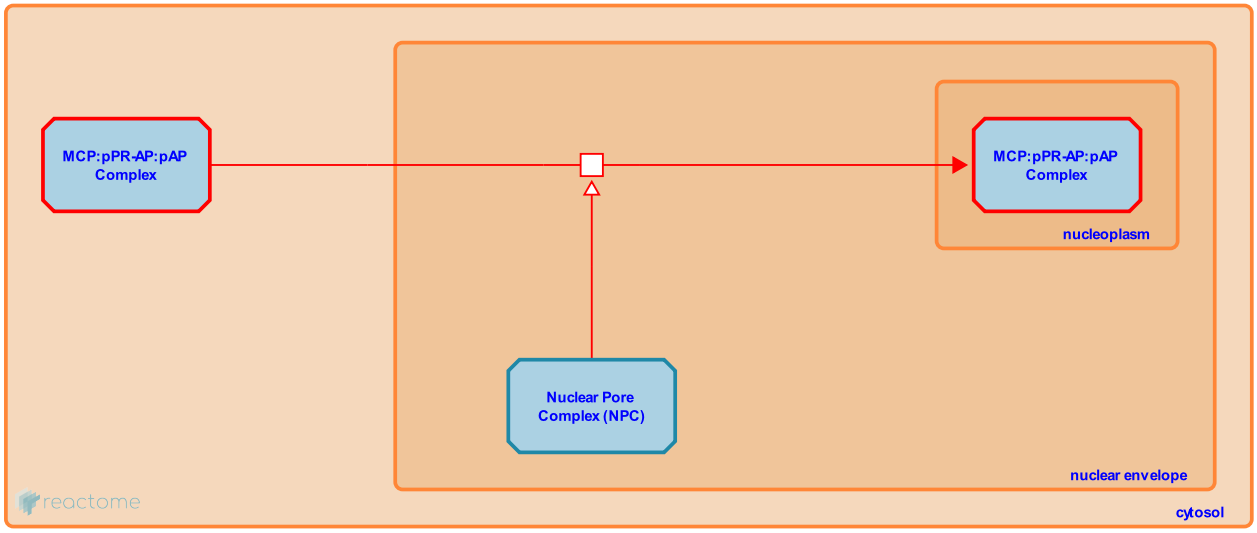
Location: HCMV Late Events

Stable identifier: R-HSA-9629004

Type: transition

Compartments: nuclear envelope

Diseases: viral infectious disease



The process of capsid continues with the rranslocation of SCP, Triplex (TRI) complex, CVC complex, and accessory proteins from the cytoplasm into the nucleous, joing MCP and the maturational protease precursor complex (pPR-AP:pAP). Together these are the structural foundation of the Procapsid.

Preceded by: Binding of the major capsid protein (MCP) to the pPR-AP:pAP complex

Followed by: pPR-AP:pAP cleaves the MCP:pPR-AP:pAP Complex

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2019-10-18	Reviewed	Streblow, DN., Caposio, P.

pPR-AP:pAP cleaves the MCP:pPR-AP:pAP Complex ↗

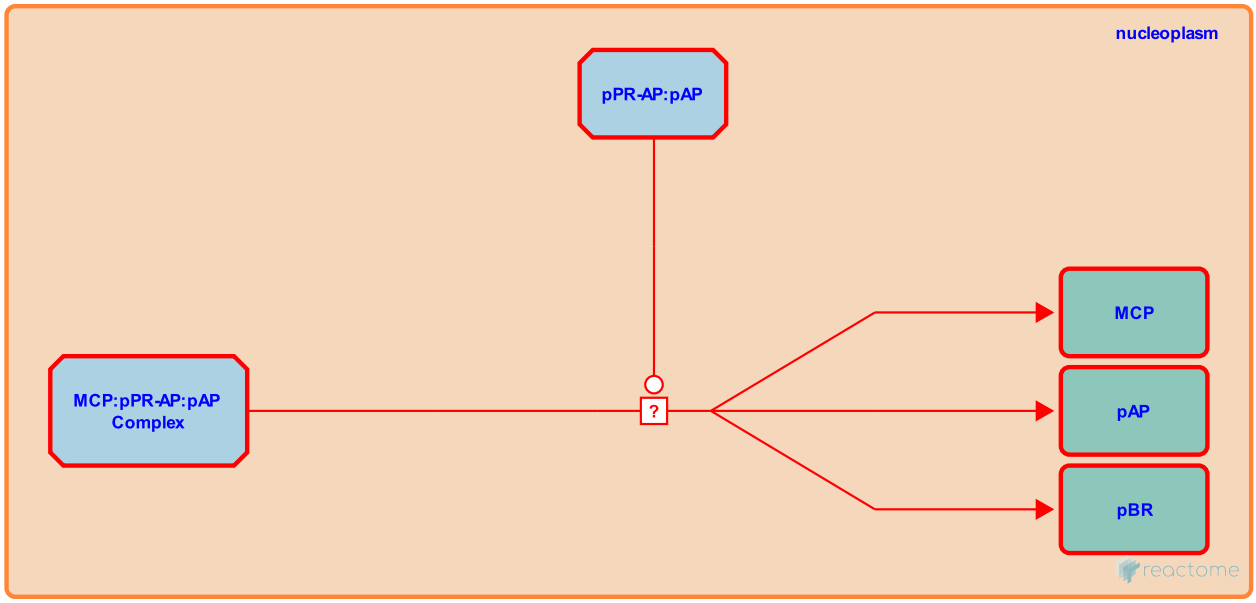
Location: HCMV Late Events

Stable identifier: R-HSA-9698929

Type: uncertain

Compartments: nucleoplasm

Diseases: viral infectious disease



The maturational protease (PR) processes both pPR-AP and pPR in a pathway that releases PR, pAP, and AP. Although pAP is sufficient for procapsid assembly, self-cleavage of pPR-AP to PR and release of a number of pAP and pPR-AP products are required for proper DNA encapsidation and production of nucleocapsids. Precise protease cleavage steps lead to the release of major capsid protein (MCP), inactivation of the protease, and orchestration of the replacement of the scaffold in procapsids with viral DNA. PR and AP, as well as pAP forms, are completely removed from nucleocapsids into which DNA has been packaged.

Preceded by: Transport of MCP:pPR-AP:pAP Complex into the Nucleous

Followed by: Translocation of SCP, Triplex (TRI) complex, CVC complex, and Accessory Proteins from the cytoplasm into the nucleous

Literature references

Howley, PM., Fields, BN., Griffin, DE., Knipe, DM. (2001). Orthomyxoviridae: The Viruses and Their Replication, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-11-28	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Translocation of SCP, Triplex (TRI) complex, CVC complex, and Accessory Proteins from the cytoplasm into the nucleous ↗

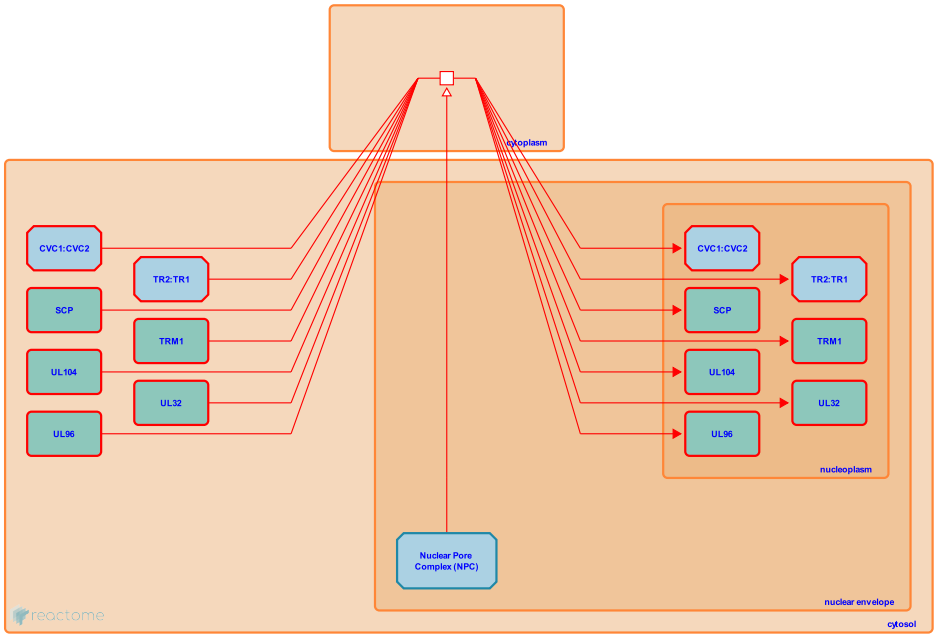
Location: HCMV Late Events

Stable identifier: R-HSA-9636128

Type: transition

Compartments: cytoplasm

Diseases: viral infectious disease



The process of capsid continues with the rranslocation of SCP, Triplex (TRI) complex, CVC complex, and accessory proteins from the cytoplasm into the nucleous, joing MCP and the maturational protease precursor complex (pPR-AP:pAP). Together these are the structural foundation of the Procapsid.

Preceded by: pPR-AP:pAP cleaves the MCP:pPR-AP:pAP Complex

Followed by: Assembly of HCMV Procapsid

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins.*

Editions

2018-11-28	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Assembly of HCMV Procapsid ↗

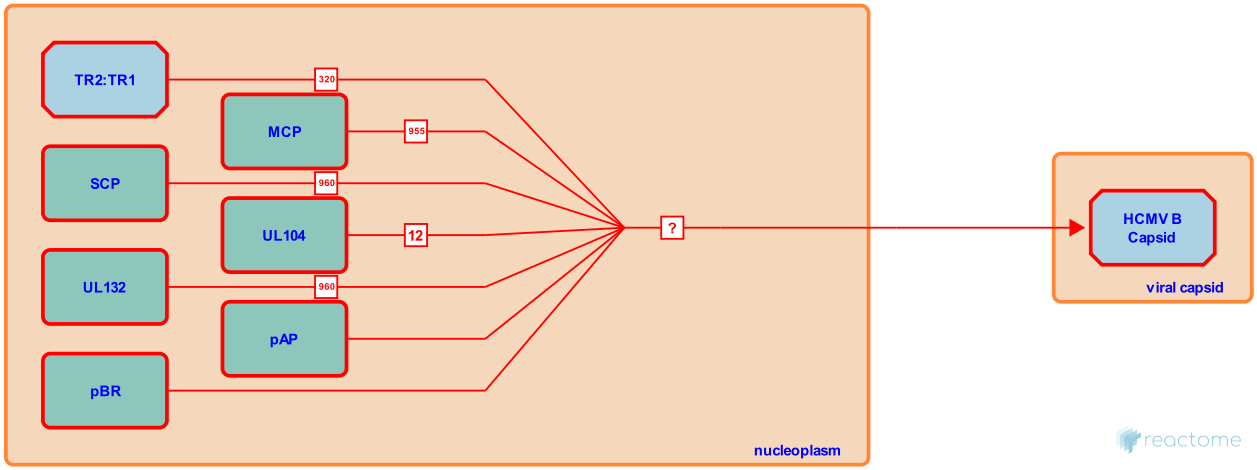
Location: HCMV Late Events

Stable identifier: R-HSA-9698932

Type: uncertain

Compartments: nucleoplasm

Diseases: viral infectious disease



The procapsid shell is made up of major capsid proteins (MCP)-containing capsomeres, with six copies of MCP per hexon and five copies of MCP per penton. One of the 12 pentons in each capsid is composed entirely of portal protein (PORT), the UL104 protein, a self-assembling homododecamer. The PORT penton provides a channel for viral DNA encapsidation. Triplex (TRI) complex TRI1:TRI2 is added to stabilize hexons and pentons, and small capsid protein (SCP)decorates the outer capsid surface, interacting with MCP at hexon tips.
Before the capsid has aquired the genome, it is designated a B capsid. Three capsid forms accumulate in the nucleus of herpesvirus-infected cells: A capsids that lack both scaffold and packaged viral DNA, B capsids that contain scaffold but lack viral DNA, and C capsids, contains viral DNA in place of scaffold and probably represents nucleocapsids in the process of maturation.

Preceded by: Translocation of SCP, Triplex (TRI) complex, CVC complex, and Accessory Proteins from the cytoplasm into the nucleous

Followed by: B Nucleocapsid Assembly, Packaging of Viral Genome Into C Capsids

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-11-28	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Packaging of Viral Genome Into C Capsids ↗

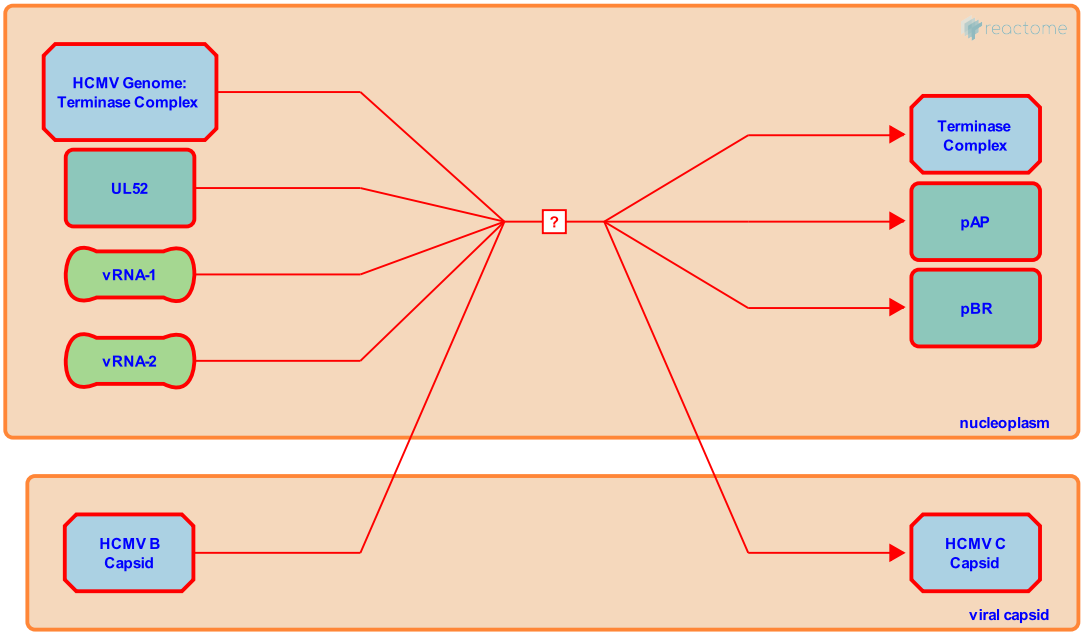
Location: HCMV Late Events

Stable identifier: R-HSA-9698925

Type: uncertain

Compartments: nucleoplasm

Diseases: viral infectious disease



The preformed procapsids are made in the nucleus proximal to DNA replication compartments. Encapsidation of unit-length viral DNA genomes depends on a terminase complex interacting with a specialized PORT penton. Terminase machinery recognizes free genomic ends and threads a single genome length of DNA through the PORT channel into each capsid. This process begins and ends at pac elements within terminal repeated a sequences, proceeding in a directional manner (S component first) on concatemeric DNA. A 129-bp region contains both cis-acting pac elements (pac1 and pac2) and is sufficient to direct cleavage and packaging leaving single-base 3′ extensions at both genomic ends.
Once the capsid has aquired the genome, it is designated a C capsid. Three capsid forms accumulate in the nucleus of herpesvirus-infected cells: A capsids that lack both scaffold and packaged viral DNA, B capsids that contain scaffold but lack viral DNA, and C capsids, contains viral DNA in place of scaffold and probably represents nucleocapsids in the process of maturation.

Preceded by: Assembly of HCMV Procapsid

Followed by: C Nucleocapsid Assembly

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins.*

Pari, GS., Prichard, MN., Penfold, ME., Bohlman, MC., St Jeor, S., Jairath, S. (1998). Identification of persistent RNA-DNA hybrid structures within the origin of replication of human cytomegalovirus. *J. Virol., 72*, 6997-7004. ↗

Editions

2018-11-28	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

B Nucleocapsid Assembly ↗

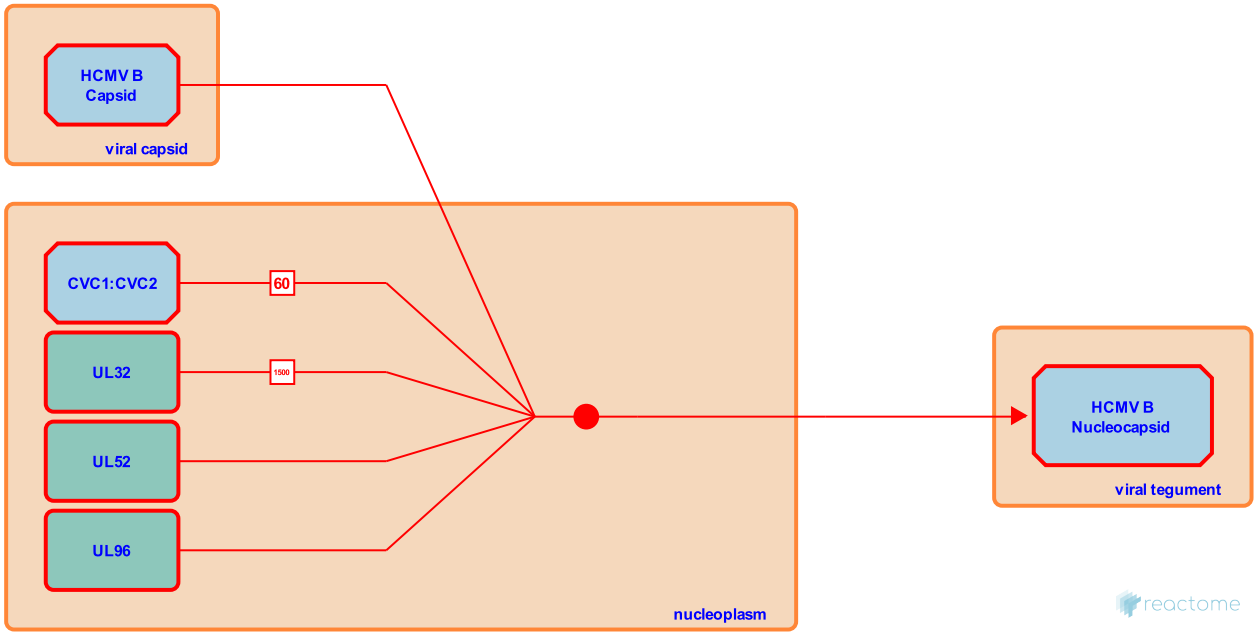
Location: HCMV Late Events

Stable identifier: R-HSA-9698924

Type: binding

Compartments: nucleoplasm

Diseases: viral infectious disease



A non-infectious B capsid aquires both tegument and transport protein in the nucleus. A putative capsid vertex capping complex (CVC), composed of UL77 (CVC1) and UL93 (CVC2) proteins, decorates penton tips, and the UL51 and UL52 proteins are added to provide capsid stability. The order of addition of capsid vertex and stabilizing proteins (UL77, UL93, UL51, and UL52) remains to be established. It is not yet resolved whether these proteins are to be considered components of the capsid or tegument. The most capsid-proximal major tegument protein in HCMV is the UL32 protein, pp150, added to nucleocapsids in the nucleus and accompanying maturing particles to the cytoplasm. The pp150 and ppUL96 proteins stabilize nucleocapsids in a common pathway of translocation to cytoplasmic sites of envelopment.

Preceded by: Assembly of HCMV Procapsid

Followed by: HCMV B Nucleocapsid Translocation

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2019-02-12	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

C Nucleocapsid Assembly ↗

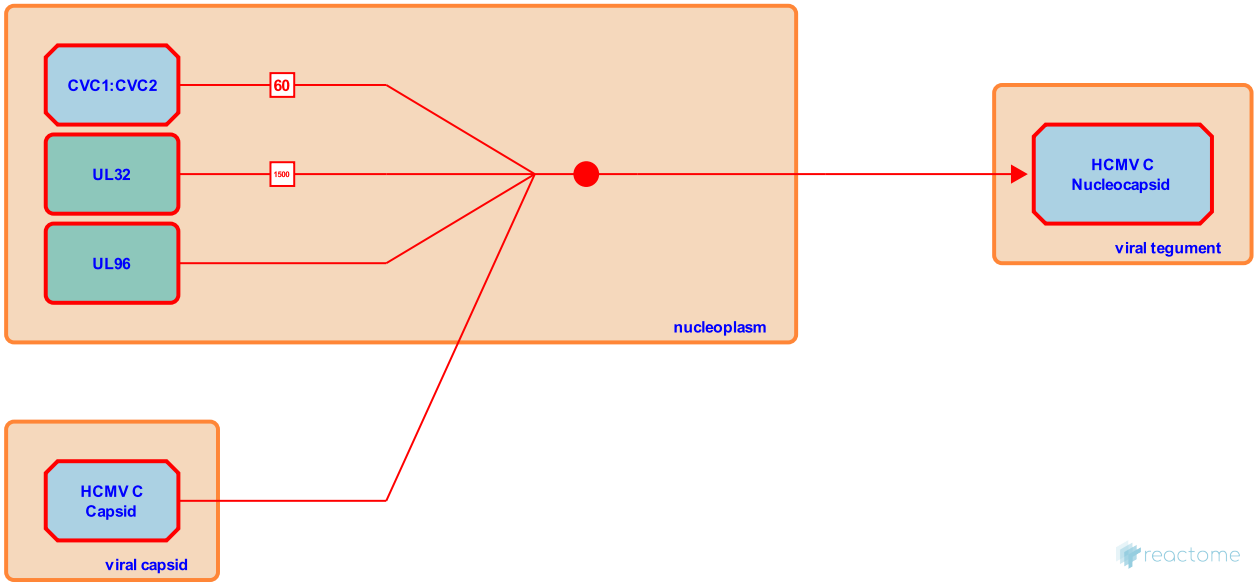
Location: HCMV Late Events

Stable identifier: R-HSA-9698931

Type: binding

Compartments: nucleoplasm

Diseases: viral infectious disease



An infectious C capsid aquires both tegument and transport protein in the nucleus. A putative capsid vertex capping complex (CVC), composed of UL77 (CVC1) and UL93 (CVC2) proteins, decorates penton tips, and the UL51 and UL52 proteins are added to provide capsid stability. The order of addition of capsid vertex and stabilizing proteins (UL77, UL93, UL51, and UL52) remains to be established. It is not yet resolved whether these proteins are to be considered components of the capsid or tegument. The most capsid-proximal major tegument protein in HCMV is the UL32 protein, pp150, added to nucleocapsids in the nucleus and accompanying maturing particles to the cytoplasm. The pp150 and ppUL96 proteins stabilize nucleocapsids in a common pathway of translocation to cytoplasmic sites of envelopment.

Preceded by: Packaging of Viral Genome Into C Capsids

Followed by: HCMV C Nucleocapsid Translocation

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins.*

Editions

2019-10-18	Reviewed	Streblow, DN., Caposio, P.
2019-11-12	Authored, Edited	Gillespie, ME.

HCMV B Nucleocapsid Translocation ↗

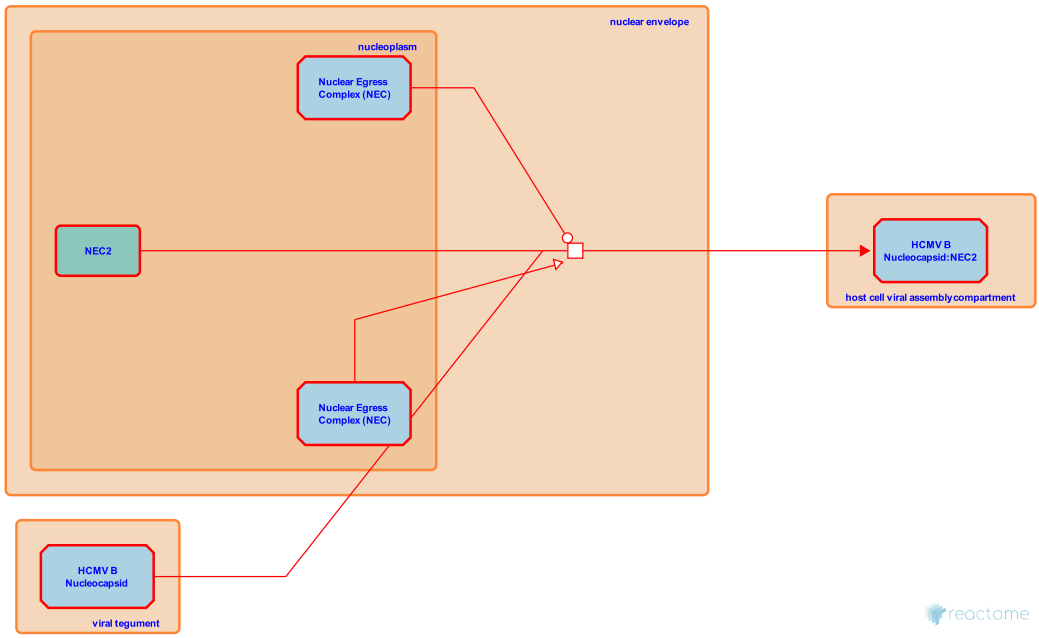
Location: HCMV Late Events

Stable identifier: R-HSA-9698933

Type: transition

Compartments: nuclear envelope

Diseases: viral infectious disease



Nucleocapsid B transport from the nucleus to the cytoplasm is carried out by a herpesvirus-conserved nuclear egress complex (NEC). The NEC is located at the inner nuclear membrane. This is probably one quality control step where preference is afforded to DNA-containing C capsids (nucleocapsids) over B capsids, possibly mediated by tegument proteins that associate with C capsids.The NEC is composed of a type II membrane-spanning component (NEC1, UL50 gene product) together with a nuclear lamina-interacting component (NEC2, UL53 gene product). This complex facilitates egress from the nucleus by recruiting cellular and viral protein kinases to phosphorylate and disrupt the nuclear lamina cage and allow nucleocapsid passage. Consistent with this, NEC1 or NEC2 mutant viruses in many herpesviruses including MCMV and HCMV accumulate nucleocapsids (C capsids) in the nucleus. In HCMV, host protein kinase C functions interchangeably with viral ppUL97/VPK, cellular p32, and the lamin B receptor in the NEC to phosphorylate lamins. Nucleocapsids are delivered to the cytoplasm with pp53/NEC2 remaining attached. ppUL53 accompanies the nucleocapsid as it is transported through the cytoplasm and becomes part of the tegument in mature virions. ppUL50/NEC1 remains in the nucleus and apparently cycles ppUL53.

Preceded by: B Nucleocapsid Assembly

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins.*

Editions

2019-02-12	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

HCMV C Nucleocapsid Translocation ↗

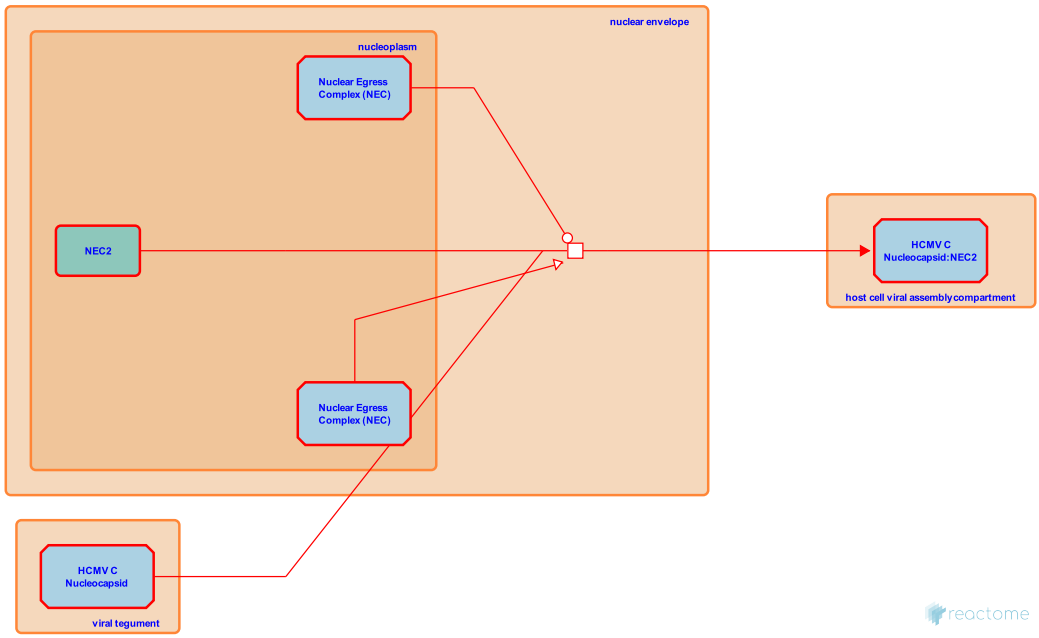
Location: HCMV Late Events

Stable identifier: R-HSA-9698930

Type: transition

Compartments: nuclear envelope

Diseases: viral infectious disease



Nucleocapsid C transport from the nucleus to the cytoplasm is carried out by a herpesvirus-conserved nuclear egress complex (NEC). The NEC is located at the inner nuclear membrane. This is probably one quality control step where preference is afforded to DNA-containing C capsids (nucleocapsids) over B capsids, possibly mediated by tegument proteins that associate with C capsids.The NEC is composed of a type II membrane-spanning component (NEC1, UL50 gene product) together with a nuclear lamina-interacting component (NEC2, UL53 gene product). This complex facilitates egress from the nucleus by recruiting cellular and viral protein kinases to phosphorylate and disrupt the nuclear lamina cage and allow nucleocapsid passage. Consistent with this, NEC1 or NEC2 mutant viruses in many herpesviruses including MCMV and HCMV accumulate nucleocapsids (C capsids) in the nucleus. In HCMV, host protein kinase C functions interchangeably with viral ppUL97/VPK, cellular p32, and the lamin B receptor in the NEC to phosphorylate lamins. Nucleocapsids are delivered to the cytoplasm with pp53/NEC2 remaining attached. ppUL53 accompanies the nucleocapsid as it is transported through the cytoplasm and becomes part of the tegument in mature virions. ppUL50/NEC1 remains in the nucleus and apparently cycles ppUL53.

Preceded by: C Nucleocapsid Assembly

Followed by: Addition of Tegument to HCMV Nucleocapsid C

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins.*

Editions

2019-02-12	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

Addition of Tegument to HCMV Nucleocapsid C ↗

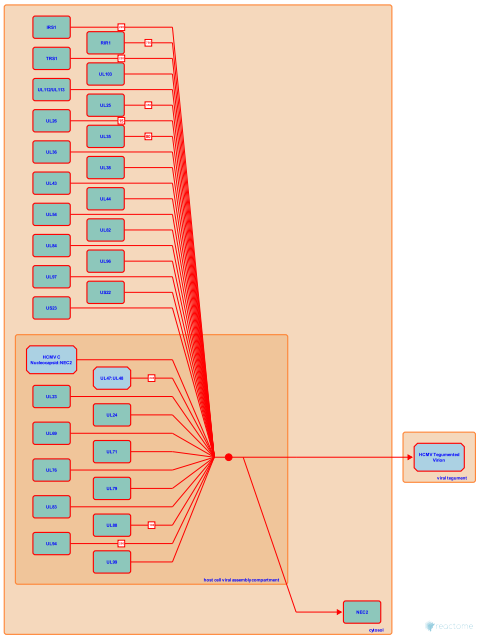
Location: HCMV Late Events

Stable identifier: R-HSA-9640368

Type: binding

Compartments: host cell viral assembly compartment

Diseases: viral infectious disease



Nucleocapsids most likely reach the cytoplasm by obtaining a temporary envelope at the inner nuclear membrane passage through the perinuclear space and de-envelopment at the outer nuclear membrane. Once delivered to the cytoplasm, further assembly occurs within the cytoplasmic viral assembly compartment (AC) composed of cellular membranes and organelles that support the final steps in maturation and release. Subsequently transport is directed to sites where tegumented nucleocapsids obtain a second, final envelope to become virions.

Preceded by: HCMV C Nucleocapsid Translocation

Followed by: HCMV Formation of Final Envelopment Complex

Literature references

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2019-03-09	Authored	Gillespie, ME.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

HCMV Formation of Final Envelopment Complex ↗

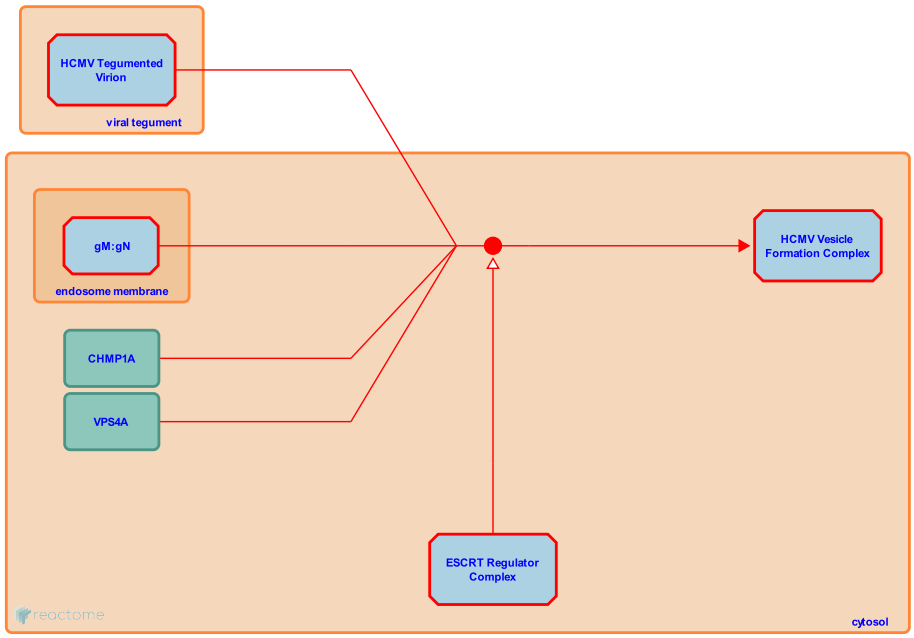
Location: HCMV Late Events

Stable identifier: R-HSA-9610942

Type: binding

Compartments: cytosol

Diseases: viral infectious disease



Both Vps4A and CHMP1A are localized in the vicinity of viral cytoplasmic assembly compartments, sites of viral maturation that develop in CMV-infected cells. Localization of CHMP1A and Vps4A proteins in the vicinity of AC, where the final steps in virus maturation and envelopment occur, indicates an important role of ESCRT pathway during these processes in HCMV life cycle. Both Vps4A and CHMP1A, the ESCRT-III component, influence the outcome of ESCRT recruitment via upstream parallel pathways using Tsg101, ALIX, or HECT-Ub ligases. Vps4A contributes to all three known primary mechanisms of ESCRT recruitment by viruses. Tsg101, a component of ESCRT-I, normally functions to deliver ubiquitinated transmembrane proteins to MVBs. ALIX binds to Tsg101 in addition to ESCRT-III protein CHMP-4B, thus linking ESCRT-I and ESCRT-III.
VPS4A and CHMP1A components localize within the assembly compartment (AC), with a striking colocalization of the chromatin modifying protein 1A (CHMP1A) and assembled gM:gN. Both the Vps4A and CHMP1A localized in the vicinity of viral cytoplasmic assembly compartments are sites of viral maturation that develop in human cytomeglovirus (HCMV)-infected cells. The accumulation of viral tegument also occurs during this step of viral maturation.

Preceded by: Addition of Tegument to HCMV Nucleocapsid C

Followed by: HCMV Final Envelopment

Literature references

Mocarski, ES., Tandon, R., AuCoin, DP. (2009). Human cytomegalovirus exploits ESCRT machinery in the process of virion maturation. *J. Virol., 83*, 10797-807. ↗

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-06-13	Authored	Guerreiro, C.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

HCMV translocates from the endosome lumen to the extracellular region ↗

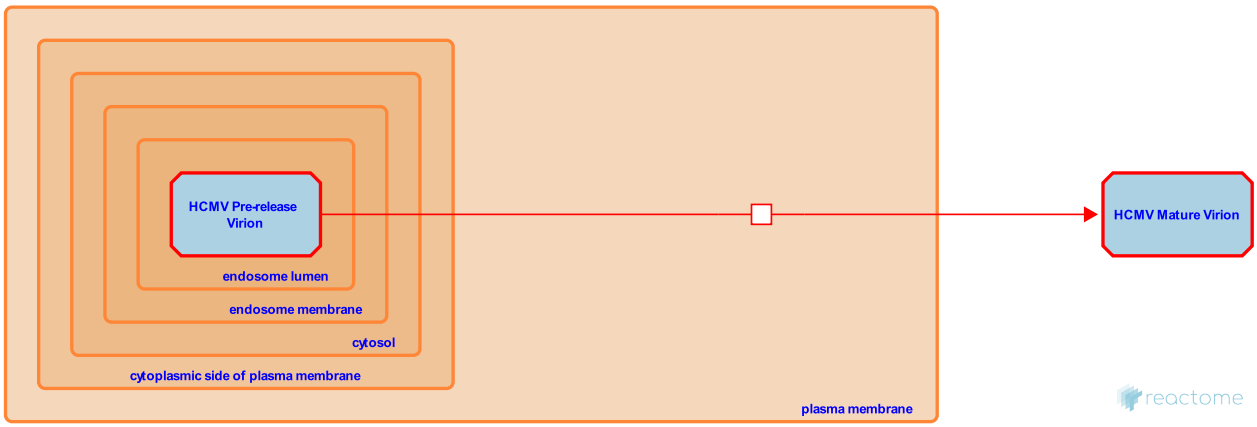
Location: HCMV Late Events

Stable identifier: R-HSA-9610388

Type: transition

Compartments: plasma membrane

Diseases: viral infectious disease



The enveloped virion is carried in a vesicle which will be released through exocytosis. This step carries virus particles as well as dense bodies to the extracellular space. The host cellular exocytic pathway carries out this process.

Preceded by: HCMV Final Envelopment

Literature references

Cannon, MJ., Schmid, DS., Hyde, TB. (2010). Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. *Rev. Med. Virol., 20*, 202-13. ↗

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-06-07	Authored	Guerreiro, C.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

HCMV Final Envelopment ↗

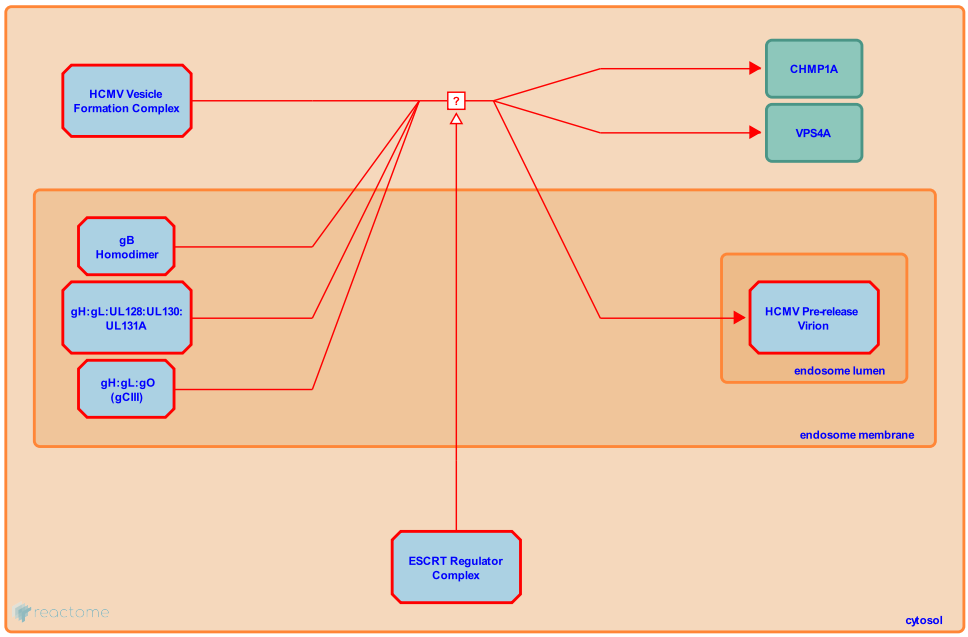
Location: HCMV Late Events

Stable identifier: R-HSA-9610954

Type: uncertain

Compartments: cytosol

Diseases: viral infectious disease



As part of the HCMV Vesicle Formation Complex, Vps4 controls the release of ESCRT complexes from membranes. Upstream ESCRT complexes ESCRT-I and ESCRT-II are believed to work in parallel to recruit the cargo, whereas Vps4 and ESCRT-III work in series. Virus envelopment occurs by budding into endosomal vesicles, which fuse with the plasma membrane to release virions to the extracellular space. Accumulation of viral glycoproteins gM-gN and ESCRT proteins at the periphery of AC support this model of viral egress, where these proteins provide essential functions such as envelopment and endosomal budding before viral exit.
Both Vps4A and CHMP1A are localized in the vicinity of viral cytoplasmic assembly compartments, sites of viral maturation that develop in CMV-infected cells. Localization of CHMP1A and Vps4A proteins in the vicinity of AC, where the final steps in virus maturation and envelopment occur, indicates an important role of ESCRT pathway during these processes in HCMV life cycle. Both Vps4A and CHMP1A, the ESCRT-III component, influence the outcome of ESCRT recruitment via upstream parallel pathways using Tsg101, ALIX, or HECT-Ub ligases. Vps4A contributes to all three known primary mechanisms of ESCRT recruitment by viruses. Tsg101, a component of ESCRT-I, normally functions to deliver ubiquitinated transmembrane proteins to MVBs. ALIX binds to Tsg101 in addition to ESCRT-III protein CHMP-4B, thus linking ESCRT-I and ESCRT-III.

Preceded by: HCMV Formation of Final Envelopment Complex

Followed by: HCMV translocates from the endosome lumen to the extracellular region

Literature references

Mocarski, ES., Tandon, R., AuCoin, DP. (2009). Human cytomegalovirus exploits ESCRT machinery in the process of virion maturation. *J. Virol., 83*, 10797-807. ↗

Knipe, DM., Howley, PM. (2013). Chapter 62 - Cytomegaloviruses, Fields Virology. *Lippincott Williams & Wilkins*.

Editions

2018-06-13	Authored	Guerreiro, C.
2019-10-18	Reviewed	Streblow, DN., Caposio, P.

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