HCMV Infection

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This is just an excerpt of a full-length report for this pathway. To access the complete report, please download it at the Reactome Textbook.

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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.

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Literature references


Reactome database release: 82

This document contains 3 pathways *(see Table of Contents)*

https://reactome.org
Herpesviruses have a unique four-layered structure: a core containing the large, double-stranded DNA genome is enclosed by an icosapentahedral capsid which is composed of capsomers. The capsid is surrounded by an amorphous protein coat called the tegument. It is encased in a glycoprotein-bearing lipid bilayer envelope.

Herpesviruses are divided into three groups: alpha-herpesviruses, beta-herpesviruses, and gamma-herpesviruses. The beta herpesviruses have a restricted host range. Their reproductive life cycle is long (days), with infection progressing slowly in cell culture systems. These viruses cause their host cells to enlarge, as exemplified by a human cytomegalovirus (HCMV) infection. These viruses can establish latent infection in secretory glands, cells of the reticuloendothelial system, and the kidneys.

Human Cytomegalovirus, or HCMV, is a common virus that infects people of all ages. In the United States, nearly one in three children are already infected with HCMV by age 5 years. Over half of adults by age 40 have been infected with HCMV. Once HCMV is in a person’s body, it stays there for life and can reactivate.

Cytomegalovirus causes three clinical syndromes:

1. Congenital cytomegalovirus infection (when symptomatic) causes hepatosplenomegaly, retinitis, rash, and central nervous system involvement.

2. In about 10 per cent of older children and adults, primary cytomegalovirus infection causes a mononucleosis syndrome with fever, malaise, atypical lymphocytosis, and pharyngitis.

3. Immunocompromised hosts (transplant recipients and human immunodeficiency virus [HIV]-infec-
ted individuals) may develop life-threatening disseminated disease involving the lungs, gastrointestinal tract, liver, retina, and central nervous system.

Experimentally HCMV can be propagated in multiple cell lines. When propagated in human fibroblasts, HCMV clinical isolates acquire mutations in a manner that suggests a process of adaptation. Two strains of HCMV AD169 (grown from cultures of adenoid tissue taken from a 7-year-old girl) and Towne (developed as an attenuated vaccine by passaging 125 times in vitro) were initially used as the primary clinical strains. As only 26% of HCMV canonical genes (45/171) are essential for viral replication in vitro it became important that a model strain be developed.

The Merlin BAC was derived for this use. Produced using a bacterial artificial chromosome (BAC) cloning system (to avoid adaptation/degradation of the genome with each passage) the Merlin strain contains a complete HCMV genome that is thought to accurately represent the original clinical agent from which it was derived. It is also a reproducible source of clonal virus (via transfection) and is capable of reconstituting phenotypically wild-type virus.

The lifecycle represented here uses the Merlin strain where possible. Infectious Human Cytomegalovirus (HCMV) particles enter the cell through interaction with cellular receptors. Once in the cytoplasm capsid and tegument proteins are delivered to the cytosol. The capsid travels to the nucleus, where the genome is delivered and circularized. Tegument proteins regulate host cell responses and initiate the expression of viral I immediate early genes. This is followed by delayed early genes, which initiate viral genome replication, then late genes. Late gene expression initiates capsid assembly in the nucleus, followed by nuclear egress to the cytosol. Capsids associate with tegument proteins in the cytosol and are trafficked to the viral assembly complex that contains components from the endoplasmic reticulum, Golgi apparatus, and endosomal machinery. The capsids acquire additional tegument proteins and a viral envelope by budding into intracellular vesicles. These vesicles fuse with the plasma membrane to release enveloped infectious particles along with non-infectious dense bodies.

**Literature references**


**Editions**

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Once in the cytoplasm the capsid and tegument proteins are free to interact with host proteins. The capsid travels to the nucleus, where the genome is delivered and circularized. Tegument proteins regulate host cell responses and initiate the expression of viral I immediate early genes. This is followed by the expression of delayed early genes.

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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.

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Table of Contents

Introduction .................................................. 1
HCMV Infection ............................................... 2
  HCMV Early Events ...................................... 4
  HCMV Late Events ....................................... 5
Table of Contents .......................................... 6