Structure and Formation of the Cytomegalovirus Virion

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Abstract  Transport and protection of the nuclear-replicating double-stranded DNA genome of herpesviruses is accomplished by the virion and its substructures. Studies of the composition, organization, and formation of these particles have provided insight into the molecular mechanisms of virus assembly, leads for antiviral strategies, and information about cellular processes that are required for, resemble, or antagonize virus replication. This chapter updates earlier reviews on the structure and formation human cytomegalovirus (HCMV) virions (Gibson 1996, 2006; Eickmann et al. 2006), and complements several other reviews on herpesvirus structure and replication presented in this volume (see the chapters by E. Murphy and T. Shenk, Z. Ruzsics and U. Koszinowski, R. Kalejta, and G.S. Pari) and elsewhere (Rixon 1993; Steven and Spear 1997; Brown et al. 2002; Varnum et al. 2004; Liu and Zhou 2007).

Introduction

For purposes of brief introduction, the general characteristics of the CMV virion can be summarized as follows. Typical of the herpesvirus group, the virion of HCMV is approximately 230 nm in diameter and is composed of a nucleocapsid, surrounded by
a less structured tegument layer, and bounded by a trilaminate membrane envelope (Fig. 1a). The HCMV genome is composed of a linear, double-stranded DNA molecule (236 kbp in wild type virus), the largest among the human herpesviruses, and over 50% larger than that of herpes simplex virus type 1 (HSV-1) (see the chapters by E. Murphy and T. Shenk, and G.S. Pari, this volume). The capsid is isosahedral and about the same diameter as that of HSV (~110 nm, depending on preparation). Accommodating a larger DNA in a similar diameter capsid may be achieved by eliminating the maturational protease (pUL80a) from the interior of CMV capsids (Chan et al. 2002; Loveland et al. 2007). The capsid is composed of four integral protein species (for HCMV, pUL46, pUL80.5, pUL85, pUL104) that are organized into 162 capsomeres (150 hexamers plus 12 pentamers) and 320 triplexes located between the capsomeres. By analogy with HSV-1, one of the pentamer positions is

**Fig. 1** Particles in cytoplasm of CMV-infected cells. Shown here are electron micrographs of a virion with DNA, capsid, tegument, and envelope indicated by arrows, b virion within small vesicle or tubule indicated by thinner arrow, c tegumented C-capsid, with coarse fibrillar material especially evident on right-hand side, budding into a vesicle or tubule (arrow) to become virion, and d tegumented B-capsid budding into large tubule or vesicle (top arrow) to become NIEP; showing thickening of vesicle membrane where apposed to particle (bottom arrow)