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Host organelle invasion: Proteomic snapshots of Human cytomegalovirus virion assembly and maturation

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Human cytomegalovirus (HCMV) is a ubiquitous human pathogen that infects over 60% of adult population. Whilst HCMV infections are generally asymptomatic in healthy individuals, it is a significant cause of morbidity and mortality in immuno-compromised people, and a major cause of birth defects. Assembly of the infectious HCMV virion is an elaborate process of considerable interest that still remains largely unknown. In the nucleus, capsid assembly and maturation precedes DNA packaging and initial nuclear tegumentation. The capsid then egresses from the nucleus and undergoes additional cytoplasmic tegumentation and secondary envelopment prior to extracellular release. Major gaps governing these later molecular events exist, including the precise cellular locations. To determine which host sites are hijacked for virion assembly and maturation, organelle isolation and fractionation was optimized in lung fibroblast MRC5 cells using Optiprep density-based separation. This was followed by collection of individual organelle fractions from each uninfected (MOCK) and HCMV infected (strain AD169) MRC5 cells at 24, 48, 72, and 96 hours post infection (hpi). Individual organelles were lysed, resolved by SDS-PAGE, and analyzed in 186 individual nLC-MS/MS, runs per biological replicate. HCMV induced comprehensive organelle remodeling including the appearance of more dense structures within infected cells at 24 hpi, which increased in abundance until 96 hpi. Of the viral proteins that are known components of the infectious virion, 18 tegument and 11 envelope proteins were identified and enriched in completely distinct subcellular localizations suggesting alternate trafficking pathways. Immunofluorescence confirmed temporal and spatial localization of critical host factors and viral proteins.

Biography

Mathias completed his Ph.D. in 2009 from The University of Melbourne, and undertook postdoctoral training with Prof. Richard Simpson at the Ludwig Institute for Cancer Research (2010-2011) studying the contribution of the extracellular microenvironment during epithelial-mesenchymal transition. In 2011 he was awarded an Australian NHMRC Early Career Fellowship, and since 2012 has been working as a postdoctoral fellow at Princeton University in the laboratory of Assoc. Prof. Ileana Cristea studying viral-host protein interactions during HCMV infection. Mathias currently has 15 peer-reviewed journal publications.