ABSTRACT

TITLE:	Regulation of Mir-132 Expression and Viral Entry in Mrc-5 Cells Via HCMV Infection and Ganciclovir Administration
AUTHOR(S):	Glade, Michael; Njenga, Melba
PRESENTED AT:	2016 Undergraduate Research and Creative Activities Symposium, Fort Lewis College

ABSTRACT: It has been reported that 50-85% of U.S. adults have been infected with human cytomegalovirus (HCMV) by the age of 40. HCMV can cause microcephaly in newborns and symptoms in immunocompromised patients (i.e., AIDS and organ or tissue transplants). HCMV is a double-stranded DNA (dsDNA) virus that infects primary fibroblasts, including MRC-5 cells. It gains entry into the host cell via receptor-mediated membrane fusion and displays both latent and lytic replication phases. The most common anti-HCMV drug is Ganciclovir (GC), which is a DNA-dependent DNA polymerase inhibitor. HCMV has been demonstrated to regulate expression of host cell microRNAs (miRNAs). Host miRNAs are small non-coding RNAs typically 20-25 nucleotides in length. They regulate post-transcriptional gene silencing by directing proteins to repress translation, which leads to mRNA degradation. The host miRNA, miR-132, has been shown to downregulate interferon-beta (IFN) in monocytes. Moreover, miR-132 is upregulated in HCMV-infected monocytes in order to hinder IFN expression thereby promoting viral entry. In other words, although miR-132 is a host-encoded molecule it downregulates the host antiviral process of IFN production and serves as an advantageous upregulation target for HCMV. This study investigated whether HCMV upregulates host miR-132 expression in MRC-5 cells and if the presence of GC reverses this upregulation thereby hindering viral entry. Cellular miR-132 levels and HCMV entry were monitored via RT-qPCR and flow cytometry, respectively. Although not statistically significant, HCMV-infected MRC-5 cells appeared to exhibit upregulation of miR-132 in comparison to control cells and GC demonstrated a trend towards reversing this HCMV-induced upregulation 24 hours post infection. Therefore, our results support previous data that HCMV infection increases miR-132 levels in MRC-5 cells. In addition, our results suggest that GC affects later processes in HCMV's replication cycle in order to counteract miR-132 regulation; however, to our knowledge the mechanism by which this process occurs is not yet understood.