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Researchers report details of new studies and findings in the area of herpesvirus

Herpesvirus data are the focus of recent research from the United States.

Study 1: The HMGB1 protein facilitates RTA-mediated viral gene expression in gamma-2 herpesviruses.

"Replication and transcription activator (RTA), an immediate-early gene product of gamma-2 herpesviruses including Kaposi's sarcoma-associated herpesvirus (KSHV) and murine gamma herpesvirus 68 (MHV-68), plays a critical role in controlling the viral life cycle.

"RTA acts as a strong transcription activator for several downstream genes of KSHV and MHV-68 through direct DNA binding, as well as via indirect mechanisms. HMGB1 (also called HMG-1) protein is a highly conserved nonhistone chromatin protein with the ability to bind and bend DNA," scientists writing in the *Journal of Virology* report.

"HMGB1 protein promoted RTA binding to different RTA target sites in vitro, with greater enhancement to low-affinity sites than to high-affinity sites. Box A or box B and homologues of HMGB1 also enhanced RTA binding to DNA," said M.J. Song and coworkers.

"Transient transfection of HMGB1

stimulated RTA transactivation of RTA-responsive promoters from KSHV and MHV-68. Furthermore," the authors continued,

"MHV-68 viral gene expression, as well as viral replication, was significantly reduced in HMGB1-deficient cells than in the wild type. This abated viral gene expression was partially restored by HMGB1 transfection into HMGB1-/- cells."

Song concluded, "These results suggest an important function of the DNA architectural protein, HMGB1, in RTA-mediated gene expression, as well as viral replication in gamma-2 herpesviruses."

Song and colleagues published their study in the *Journal of Virology* (The DNA architectural protein HMGB1 facilitates RTA-mediated viral gene expression in gamma-2 herpesviruses. *J Virol*, 2004;78(23):12940-12950).

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Study 2: Immediate-early expression of the herpes simplex virus type 1 ICP27 transcript is not critical for efficient replication in vitro or in vivo.

"We constructed a promoter mutation altering the immediate-early expression of the herpes simplex virus type 1 (HSV-1) ICP27 transcript and its cognate wild-type rescue viruses in order to assess the role of the ICP27 protein in the earliest stages of viral infection by global transcriptional analysis with a DNA microarray. This mutant, ICP27/VP16, replaces the whole ICP27 promoter/enhancer with the VP16 promoter. It demonstrates loss of immediate-early expression of ICP27 according to the criteria expression in the absence of de novo protein synthesis and earliest expression in the kinetic cascade," scientists writing in the *Journal of Virology* report.

"Significant differences in relative transcript abundances between the mutant and wild-type rescue viruses were limited at the earliest times measured and not evident at all by four hours after infection," said Aixu Sun at the University of California-Irvine and collaborators in the U.S. "Consistent with this observation, levels of some critical proteins were reduced in the mutant as compared to rescue virus infections at the earliest times tested, but were equivalent by eight hours postinfection. Further, both single and multistep levels of virus replication were equivalent with both mutant and rescue viruses."

"Thus, altering the immediate-early kinetics of ICP27 leads to a suboptimal quantitative lag phase in gene expression but without consequence for replication fitness in vitro," stated the researchers. "Infections in vivo also revealed equivalent ability of mutant and rescue viruses to invade the central nervous system of mice following footpad injections. Limitations to an immediate-early role of ICP27 in the biology of HSV are discussed in light of these observations."

Sun and associates published their study in the *Journal of Virology* (Immediate-early expression of the herpes simplex virus type 1 ICP27 transcript is not critical for efficient replication in vitro or in vivo. *J Virol*, 2004;78(19):10470-10478).

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Study 3: Kaposi sarcoma-associated herpesvirus immediate early gene activity is explored.

According to a recent review in the journal *Frontiers in Bioscience*, "KSHV is the causative agent of three human proliferative disorders: Kaposi's sarcoma, primary effusion lymphoma and multicentric Castleman's disease."

"Herpesvirus gene expression and viral replication is a complex, tightly regulated process involving latent,

immediate early, early, and late viral gene transcription. The immediate early genes generally code for transcriptional activators and are critical for initiating viral transcription," said V. Lacoste and colleagues.

"KSHV encodes for approximately nine immediate early gene products," wrote investigators, "including ORF50, K8, K9, K3, K5, ORF57, ORF29b, ORF45, and K4.2."

"This review will address the activities of these proteins and what roles they play in virus replication, evasion of the host immune response, and viral pathogenesis," the authors concluded.

Lacoste and colleagues published their study in *Frontiers in Bioscience* (Kaposi's sarcoma-associated herpesvirus immediate early gene activity. *Front Biosci*, 2004;9(Suppl. S):2245-2272).

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The information in this article comes under the major subject areas of Herpesvirus, Kaposi Sarcoma, Immediate Early Genes, and Proteomics.

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