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Research paper

Genome-wide expression analysis reveal host genes involved in immediate-early infections of different sheeppox virus strains

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ABSTRACT

This study explored the transcriptome of lamb testis cells infected with sheeppox virus (SPPV) wild strain (WS) and vaccine strain (VS) at an immediate-early time. Most of the differentially expressed genes (DEGs) and differentially expressed highly connected (DEHC) gene network were found to be involved in SPPV-VS infection compared to SPPV-WS. Further, the signaling pathways were mostly involved in SPPV-VS infection than SPPV-WS. SPPV modulates the expression of several important host proteins such as CD40, FAS, ITGβ1, ITGα1, Pak1, Pak2, CD14, ILK leading to viral attachment and entry; immune-related DEGs such as MAPK, JNK, ERK, NFKB, IKB, PI3K, STAT which provide optimal cellular condition for early viral protein expression; and FOXO3, ATF, CDKNA1, TCF, SRF, BDNF which help in inducing apoptosis and MPTP, BAD and Tp53 inhibits apoptosis or cell death at the immediate-early time. The results captured the specific genes and enabled to understand distinct pathogenic mechanisms employed by VS and WS of SPPV.

1. Introduction

Sheeppox virus (SPPV), an infectious and contagious systemic viral disease causing agent of sheep, is grouped under the Poxviridae family and *Capripoxvirus* (CaPV) genus. Regardless of the variants of SPPV found throughout the world, historically the epidemic distribution has been the most in Africa, Middle East, and Asia (Mahmoud and Khafagi, 2016; Hajjou, 2017). The infectivity (mortality and morbidity) rate also varies with the geographical region, breed, and age group of the animal as well as strains of the virus. SPPV is one of the largest (170–260 nm × 300–450 nm), enveloped double-stranded DNA viruses. Previous studies have revealed that poxvirus genes are expressed in a cascade-like mechanism at immediate-early, early, intermediate, and late time (0.5, 1.5, 2, 8hrs respectively) in host cell cytoplasm (Assarsson et al., 2008; Satheshkumar and Moss, 2008; Yang et al., 2010; Moss, 2013). The SPPV virion binds to the glycosaminoglycans on the cell surface as a cell surface viral receptor and enters the cell cytoplasm. Pox virus immediately expresses its early genes, and these early proteins are involved in the viral DNA replication in the host cell cytoplasm. These early pox virus proteins (VETF-82 kDa, VETF-70 kDa, capping enzyme, TBP, etc.) participate in the transcription of the intermediate and late viral genes (Broyles, 2003). The early infection of the poxvirus activates first line of defense mechanism (innate immune response against the pathogen) in the host cells. The viral entry to the cell cytoplasm and host cell immune response depends on the cell type and often virulence of the virus strains (Carter et al., 2005). Therefore, we hypothesized that the immediate-early time point of host-virus interaction may alter the gene regulation and their functions in several ways, for example, cell receptor (up-/down- regulation of the different cell receptors in different signaling pathways to smooth virus entry and initiation of viral machinery), immunogenic pathways (activation/deactivation of host defense mechanism), and cell survivability by blocking apoptosis, etc. The

Abbreviations: CaPV, Capripox virus; DEG, Differentially expressed gene; DEHC, Differentially expressed highly connected; IPA, Ingenuity pathway analysis; LTC, Lamb Testis Cell; PPI, Protein-protein interaction; SPPV, Sheeppox virus; VS, Vaccine Strain; WS, Wild Strain; VETF, Viral early transcription factor; TBP, Transcription binding protein; MOI, Multiplicity of infection.

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