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Gene expression analysis of whole blood RNA from pigs infected with low and high pathogenic African swine fever viruses

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African swine fever virus (ASFV) is a macrophage-tropic virus responsible for ASF, a transboundary disease that threatens swine production world-wide. Since there are no vaccines available to control ASF after an outbreak, obtaining an understanding of the virus-host interaction is important for developing new intervention strategies. In this study, a whole transcriptomic RNA-Seq method was used to characterize differentially expressed genes in pigs infected with a low pathogenic ASFV isolate, OUR T88/3 (OURT), or the highly pathogenic Georgia 2007/1 (GRG). After infection, pigs infected with OURT showed no or few clinical signs; whereas, GRG produced clinical signs consistent with acute ASF. RNA-Seq detected the expression of ASFV genes from the whole blood of the GRG, but not the OURT pigs, consistent with the pathotypes of these strains and the replication of GRG in circulating monocytes. Even though GRG and OURT possess different pathogenic properties, there was significant overlap in the most upregulated host genes. A small number of differentially expressed microRNAs were also detected in GRG and OURT pigs. These data confirm previous studies describing the response of macrophages and lymphocytes to ASFV infection, as well as reveal unique gene pathways upregulated in response to infection with GRG.

African swine fever (ASF) is a highly pathogenic transboundary disease of domestic and wild pigs caused by the ASF virus (ASFV). ASFV is endemic in parts of Africa, where it exists in a complex transmission cycle involving soft ticks, as well as direct pig-to-pig transmission¹. After being eradicated from mainland Europe in 1995, ASF re-emerged in the Caucasus in 2007 and has subsequently spread to domestic pigs and wild boar in Europe. There are no effective treatments or vaccines available so disease control is based on the enforcement of strict quarantine and stamping out measures^{2,3}. Impacts of ASFV infection include increased mortality and morbidity, loss of trade, and the costs associated with outbreak response and eradication measures. The presence and spread of ASFV in Europe and continued transmission in Africa makes the threat of ASF a global concern.

ASFV is an enveloped virus that contains a 170–190 kb double stranded DNA genome encoding 150–167 genes. It is the only member of the family *Asfarviridae*, genus *Asfivirus*. Viral proteins participate in nucleotide metabolism, transcription, DNA replication and repair, virion structure, morphogenesis and the modulation of host immunity⁴. Several open reading frames code for genes of unknown function. The virion is composed of between 30 and 50 polypeptides. Among them, 21 have been identified as structural proteins⁵. Virulence of virus strains ranges from highly pathogenic, causing death within a few days, to low pathogenic, causing sub-clinical or persistent infection with low levels of morbidity and mortality. The virus primarily targets cells of the mononuclear phagocyte system, including monocytes that circulate in the blood^{6–9}. It is the unique interaction between ASFV and its host macrophage that determine the pathogenic outcome.

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