RESEARCH ABSTRACT
SWINE HEALTH

Title: Investigating the role of PB1-F2 in the pathogenicity of circulating strains of SIV – **NPB #10-161**

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Date Submitted: 8/18/2012

SCIENTRIFIC ABSTRACT

The influenza A PB1-F2 protein is translated through a second open reading frame (ORF) in the PB1 gene segment and has been implicated in regulation of polymerase activity, immunopathology, susceptibility to secondary bacterial infection, and induction of apoptosis. The majority of work examining PB1-F2 function in infection has been performed with human and avian isolates. As the recent H1N1 2009 pandemic highlighted, swine origin influenza viruses have the capacity to infect human hosts on a large scale. Thus, it is necessary to have a proper understanding of the potential risk that pathogenicity factors from swine isolates may have on both human and swine health. Studies examining PB1-F2 from swine isolates have been focused primarily on pH1N1 viruses, which does not naturally express PB1-F2, that were engineered to encode a PB1-F2 ORF. These recombinant viruses were then studied to determine the impact of swine origin PB1-F2 on replication and pathogenicity. However, to our knowledge, experimental evidence of pH1N1 PB1-F2 protein expression from recombinant viruses has not been demonstrated. In this study we have found that PB1-F2 proteins from swine and human isolate influenza viruses have substantial differences in their cellular localization patterns and expression levels during viral infection. We provide compelling evidence that PB1-F2 protein expression is regulated at the translational level with swine isolate PB1-F2 expressed at very low levels relative to human isolate PB1-F2. Translational regulation of PB1-F2 expression was mapped to two independent regions within the PB1 mRNA, with one located within the PB1-F2 ORF and the other located downstream of the PB1-F2 ORF. Our data suggest that the presence of an intact PB1-F2 protein coding sequence alone is not predictive of PB1-F2 expression in infected cells and instead, PB1-F2 expression is differentially regulated at the translational level in an isolate-specific manner dependent on RNA sequences present in the PB1 gene.