

Ingenuity[®] Science Spotlight:

Articles featured in the Ingenuity Science Spotlight represent some of the best and most diverse examples of how IPA[®] has contributed to research across multiple platforms, research areas, and research goals.



Whole Genome Expression Profiling Reveals that Inhibition of Host Innate Immune Response Pathways by Ebola Virus can be Reversed by a Single Amino Acid Change in the VP35 Protein.

Hartman AL, Ling L, Nichol ST, Hibberd ML. J Virol. 2008 Mar 19 [Epub ahead of print].

<http://www.ncbi.nlm.nih.gov/pubmed/18353943?ordinalpos=1&itool=EntrezSystem2.PEnt>

Researchers from the Special Pathogens Branch of the Centers of Disease Control and Prevention in Atlanta, Georgia, and the Genome Institute of Singapore used IPA to analyze the differentially expressed genes related to the inhibition of host innate immune response pathways by Ebola virus. In this study, they used two strains of reverse-genetics-generated Ebola viruses to investigate the global host cell responses resulting from the inhibition of Interferon regulatory factor 3 (IRF-3) phosphorylation. One strain had the Wild type (WT) VP35 protein and the second strain had a single amino acid substitution in the IRF-3 inhibitory domain of VP35 protein at position 312 (Arginine to alanine, R312A).

Using IPA canonical pathways, from the sixty-nine genes that were commonly expressed in the cells infected with both the WT and R312A virus strains, they were able to identify that the genes TANK and caspase-6 were involved in the activation of death receptor signaling pathway. They analyzed thirty-nine genes that were uniquely expressed in cells infected with the mutant virus strain R312A and found that the genes related to innate antiviral immunity included MDA-5, RANTES, ISG15, STAT1, IRF-9, OAS, MX1, ISG54, and ISG-56. IPA canonical pathways showed that the Interferon Signaling Pathway (IFN) was most significant and activated in the mutant strain infected cells, indicating that the mutant virus was unable to suppress the IFN signaling pathway. Further investigation of the genes involved in the IFN signaling pathway along with 3 additional genes (MCP-1, RIG-1, ISG-60) that were identified as significant by IPA confirmed the array analysis results by Taqman Low density Array analysis (TLDA) and ELISA.