

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.



Identification of differentially activated cell-signaling networks associated with pichinde virus pathogenesis by using systems kinomics.

Bowick GC, Fennewald SM, Scott EP, Zhang L, Elsom BL, Aronson JF, Spratt HM, Luxon BA, Gorenstein DG, Herzog NK. J Virol. 2007 Feb;81(4):1923-33.

http://www.eurekalert.org/pub_releases/2007-02/uotm-nsm021407.php

A research team from UTMB took a unique approach to unraveling the molecular basis of how viruses induce cell-signaling changes that lead to clinical disease. They employed a kinomics assay to globally assess protein phosphorylation and kinase activity in response to infection with attenuated or virulent strains of Pichinde virus. Biological interpretation of differential host responses using IPA identified key nodes in cell-signaling pathways that may provide novel targets for antiviral therapies.

The UTMB team infected guinea pigs with attenuated and lethal variants of Pichinde virus to dissect the changes in cell-signaling networks that lead to differing outcomes of infection – namely clearance of pathogen or clinical disease. (Pichinde virus infection of guinea pigs produces a similar pathology to Lassa fever in humans, which is a CDC category A biothreat agent). Following infection, they assayed changes in peptide phosphorylation and then analyzed those global molecular responses in IPA. IPA's Canonical Pathway Analysis and computationally generated networks revealed that the insulin receptor, epidermal growth factor receptor, protein kinase C α and retinoblastoma protein may all be key factors in regulating the markedly different host responses to attenuated and lethal variants.

By incorporating IPA into their data analysis and interpretation step, the UTMB team gained a better understanding of the molecular events responsible for clinical disease, which may lead to rational drug design to inhibit microbial pathogenesis at the level of host response. IPA also enabled them to focus future investigations toward pathways and proteins that are likely to be key players in mediating pathogenesis.