

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.



Proteomic Modeling for HIV-1 Infected Microglia-Astrocyte Crosstalk.

Wang T, Gong N, Liu J, Kadiu I, Kraft-Terry SD, Mosley RL, Volsky DJ, Ciborowski P, Gendelman HE. PLoS ONE. 2008 Jun 25;3(6):e2507.

<http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0002507>

Researchers from the United States and China studied the effects of astrocytes on HIV-1 infected Microglia. In this study they hypothesized that astrocyte-Microglial cross talk contributes to the control of HIV mediated neuropathogenesis. They used IPA to analyze molecules identified by profiling the microglial proteome and found significant correlations with cellular assembly and organization and cell death networks.

Sixty-eight microglial proteins identified from the infected microglia-astrocyte co-culture group were uploaded into IPA along with their fold change values. IPA network analysis revealed 2 networks, one associated with cell assembly and organization and the second associated with cell death. In the network associated with cell assembly and organization they were able to uncover two interesting molecules, Actins and NFkB. Actins play a crucial role in cell locomotion. Microglial actins in astrocyte-co-cultures were down-regulated after HIV-1/VSV infection and the proteins related to actin binding, polymerization and stability, including MARCKS, moesin, Wiskott-Aldrich syndrome protein (WAS) and gelsolin, were all up-regulated. The down-regulation of these proteins suggests a less migratory phenotype after infection.

They were able to validate these findings in IPA through morphological and immunochemical quantification. IPA indicated that 8 of the microglial protein changes in infected microglia were related to increased cell death in eukaryotic cells. Those down-regulated proteins included annexin A1, adenomatous polyposis coli protein, sarcoplasmic reticulum 2+-Ca-ATPase, enolase-a, GMFB and galectin-3; while up-regulated proteins included programmed cell death 6-interacting protein and PP2A. Interestingly, 6 of the protein changes associated with attenuation of cell death were down-regulated including galectin-3 and peroxiredoxin-1, whereas gelsolin, moesin, cyto villin and programmed cell death 6-interacting protein were up-regulated. Further studies using Caspases as a marker for cell death induction were performed to validate microglial cell death pathways implicated by IPA network analysis.