

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.



Cell-specific expression and pathway analyses reveal alterations in trauma-related human T cell and monocyte pathways

Krzysztof Laudanski, Carol Miller-Graziano, Wenzhong Xiao, Michael N. Mindrinos, Daniel R. Richards, Asit De, Lyle L. Moldawer, Ronald V. Maier, Paul Bankey, Henry V. Baker, Bernard H. Brownstein, J. Perren Cobb, Steve E. Calvano, Ronald W. Davis, Ronald G. Tompkins, and Inflammation and Host Response to Injury Large-Scale Collaborative Research Program. Proc Natl Acad Sci U S A. 2006 Oct 17;103(42):15564-9.

<http://www.pnas.org/cgi/content/full/103/42/15564>

Researchers from the Inflammation and Host Response to Injury Large-Scale Collaborative Research Program set out to understand how the human body's overreaction to a traumatic injury can cause even more damage than the initial trauma - namely, multiple organ dysfunction syndrome. Their integrated approach of cell-specific genome-wide gene expression analysis coupled with IPA led to the discovery of pathways that are specifically perturbed in T cell populations in patients with severe trauma, offering a mechanistic explanation for the immunological dysfunction observed in patients.

The research team compared blood from trauma victims in the midst of organ failure with that of healthy people, and found that severe injuries triggered a pattern of gene expression changes in several hundred genes. Analysis of these gene expression changes in IPA enabled the researchers to build a cellular model of T cell-specific gene interactions that were significantly perturbed in trauma patients vs. healthy subjects. In particular, the identification of alterations in expression of T cell genes involved in apoptosis and energy pathways offered a mechanistic explanation for the severe injury pathology observed in trauma patients. By isolating highly enriched cell populations from the blood of severely injured patients they were able to demonstrate how genome-wide expression patterns interpreted using IPA can facilitate the understanding of the host immunological response to severe injury. Their findings highlight an experimental approach that can be broadly applied to the discovery and deconstruction of signaling pathways and regulatory networks perturbed in patient populations.